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<b>(21) International Application Number:</b> <b>PCT/US98/16905</b> <b>(22) International Filing Date:</b> <b>14 August 1998 (14.08.98)</b> <b>(30) Priority Data:</b> <table><tr><td>60/055,784</td><td>15 August 1997 (15.08.97)</td><td>US</td></tr><tr><td>60/064,926</td><td>7 November 1997 (07.11.97)</td><td>US</td></tr><tr><td>60/065,367</td><td>12 November 1997 (12.11.97)</td><td>US</td></tr><tr><td>09/071,715</td><td>1 May 1998 (01.05.98)</td><td>US</td></tr><tr><td>09/084,471</td><td>22 May 1998 (22.05.98)</td><td>US</td></tr></table> <b>(71) Applicant:</b> <b>ONCORMED, INC. [US/US]; 205 Perry Parkway, Gaithersburg, MD 20877 (US).</b> <b>(72) Inventors:</b> <b>MURPHY, Patricia, D.; 16 Stockbridge Road, Slingerlands, NY 12159-0639 (US). WHITE, Marga, B.; 8323 Sharon Drive, Frederick, MD 21704 (US). RABIN, Mark, B.; 1516 Defoe Street, Rockville, MD 20850 (US). OLSON, Sheri, J.; 2854 Yarling Court, Falls Church, VA 22042 (US). YOSHIKAWA, Matthew; 19300 Circle Gate Drive, Germantown, MD 20874 (US). JACKSON, Geoffrey, M.; 3312 Major Denton Drive, Beltsville, MD 20705 (US). ESKANDARI, Tara; 5440 Marinelli Road, Rockville, MD 20852 (US). SCHRAYER, Brenda; 4240 S. Harbor Boulevard, Oxnard, CA 93035 (US). PARK, Michael; 770 Ivy League Lane, Rockville, MD 20850 (US).</b>			60/055,784	15 August 1997 (15.08.97)	US	60/064,926	7 November 1997 (07.11.97)	US	60/065,367	12 November 1997 (12.11.97)	US	09/071,715	1 May 1998 (01.05.98)	US	09/084,471	22 May 1998 (22.05.98)	US	<b>(74) Agent:</b> <b>HALLUIN, Albert, P.; Howrey &amp; Simon, Box 34, 1299 Pennsylvania Avenue N.W., Washington, DC 20004 (US).</b>  <b>(81) Designated States:</b> <b>AU, CA, IL, JP, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).</b>  <b>Published</b> <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
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<b>(57) Abstract</b> <p>Five DNA and protein sequences have been determined for the BRCA2 gene, as have been ten polymorphic sites and their rates of occurrence in the normal alleles of BRCA2. The sequences BRCA2<sup>(om1-5)</sup> and the ten polymorphic sites will provide accuracy and reliability for genetic testing. One skilled in the art will be able to avoid misinterpretations of changes in the gene and/or protein sequence, determine the presence of a normal sequence, and of mutations of BRCA2. This invention is also related to a method of performing gene therapy with BRCA2<sup>(om1-5)</sup> coding sequences or fragments thereof. This invention is further related to protein therapy with BRCA2<sup>(om1-5)</sup> proteins or their functional equivalents.</p>																		

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## CODING SEQUENCE HAPLOTYPES OF THE HUMAN BRCA2 GENE

This is an U.S. utility patent application based on U.S. Provisional Application Serial Nos. 60/055,784 filed on August 15, 1997, 60/064,926 filed  
5 on November 7, 1997, and 60/065,367 filed on November 12, 1997.

**FIELD OF THE INVENTION**

This invention relates to a gene which has been associated with breast cancer where the gene is found to be mutated. More specifically, this  
10 invention relates to five unique coding sequences of BRCA2 gene  
BRCA2<sup>(omi1)</sup>, BRCA2<sup>(omi2)</sup>, BRCA2<sup>(omi3)</sup>, BRCA2<sup>(omi4)</sup>, and BRCA2<sup>(omi5)</sup> identified in human subjects which define five novel haplotypes.

**BACKGROUND OF THE INVENTION**

15 It has been estimated that about 5-10% of breast cancer is inherited (Rowell, S., *et al.*, *American Journal of Human Genetics* 55:861-865 (1994)). The first gene associated with both breast and ovarian cancer was cloned in 1994 from chromosome 17 by Miki, Y., *et al.*, *Science* 266:66-71 (1994). A second high-risk breast cancer conferring gene was located on chromosome  
20 13 in 1994 (Wooster, R., *et al.*, *Science* 265:2088-2090) and subsequently cloned in 1995 (Wooster, R., *et al.*, *Nature* 378:789-792). Mutations in this "tumor suppressor" gene are thought to account for roughly 35% of inherited breast cancer and 80-90% of families with male breast cancer.

Locating one or more mutations in the BRCA2 region of chromosome  
25 13 provides a promising approach to reducing the high incidence and mortality associated with breast cancer through the early detection of women and men at high risk. These individuals, once identified, can be targeted for more aggressive prevention programs. Screening is carried out by a variety of methods which include karyotyping, probe binding and DNA sequencing.

30 In DNA sequencing technology, genomic DNA is extracted from whole blood and the coding regions of the BRCA2 gene are amplified. Each of the coding regions may be sequenced completely and the results are compared to the normal DNA sequence of the gene. Alternatively, the coding sequence of the sample gene may be compared to a panel of known mutations or other

screening procedure before completely sequencing the gene and comparing it to a normal sequence of the gene.

The BRCA2 gene is divided into 27 separate exons. Exon 1 is noncoding, in that it is not part of the final functional BRCA2 protein product.

5 The BRCA2 coding region spans roughly 10433 base pairs (bp) over 70 kb. Each exon consists of 100-600 bp, except for exons 10, 11 and 27. The full length mRNA is 11-12 kb. To sequence the coding region of the BRCA2 gene, each exon is amplified separately and the resulting PCR products are sequenced in the forward and reverse directions. Because exons 10, 11, and

10 27 are so large, we have divided them into three, twenty-one, and two overlapping PCR fragments (respectively) of approximately 250-625 bp each (segments "A" through "C" of exon 10, "A" through "U" of exon 11, and "A" through "B" of exon 27).

Many mutations and normal polymorphisms have already been reported in the BRCA2 gene. A world wide web site has been built to facilitate the detection and characterization of alterations in breast cancer susceptibility genes. Such mutations in BRCA2 can be accessed through the Breast Cancer Information Core (BIC) at

15 [http://www.nhgri.nih.gov/Intramural\\_research/Lab\\_transfer/Bic](http://www.nhgri.nih.gov/Intramural_research/Lab_transfer/Bic). This data site became publicly available on November 1, 1995. Friend, S. *et al. Nature Genetics* 11:238, (1995). The information on BRCA2 was added in February, 1996.

20

The genetics of Breast Cancer Syndrome is autosomal dominant with reduced penetrance. In simple terms, this means that the syndrome runs through families: (1) both sexes can be carriers (mostly women get the

25 disease but men can both pass it on and occasionally get breast cancer); (2) most generations will likely have breast cancer; (3) occasionally women carriers either die young before they have the time to manifest disease (and yet have offspring who get it) or they never develop breast or ovarian cancer

30 and die of old age (the latter people are said to have "reduced penetrance" because they never develop cancer). Pedigree analysis and genetic counseling is absolutely essential to the proper workup of a family prior to any lab work.



Until now, the only sources of genomic sequence information for BRCA2 were GenBank (Accession Number U43746), or through the Breast Information Core (BIC) database on the Internet which requires membership in the BIC consortium. However, based upon the disclosure of this patent application, in neither GenBank nor BIC were the sequences identified and listed entirely accurate. There is a need in the art to correct these mistakes which otherwise may lead to misinterpretation of the sequence data from the patient as abnormal when it was not, or vice versa.

In addition, there is a need in the art to have available a functional allele profile which represents the most likely BRCA2 sequences to be found in the majority of the normal population. This functional allele profile is based upon frequent polymorphisms and the correct backbone sequence. The knowledge of several common normal haplotypes will make it possible for true mutations to be easily identified or differentiated from polymorphisms. Identification of mutations of the BRCA2 gene and protein would allow more widespread diagnostic screening for hereditary breast cancer than is currently possible.

The use of these common normal haplotypes, in addition to the previously published BRCA2 sequence, will reduce the likelihood of misinterpreting a "sequence variation" found in the normal population with a pathologic "mutation" (i.e. causes disease in the individual or puts the individual at a high risk of developing the disease). With large interest in breast cancer predisposition testing, misinterpretation is particularly worrisome. People who already have breast cancer are asking the clinical question: "is my disease caused by a heritable genetic mutation?" The relatives of the those with breast cancer are asking the question: "Am I also a carrier of the mutation my relative has? Thus, is my risk increased, and should I undergo a more aggressive surveillance program?"

### **SUMMARY OF THE INVENTION**

The present invention is based on the discovery of the correct genomic BRCA2 sequence and five novel sequence haplotypes found in normal human subjects of the BRCA2 gene.

It is an object of this invention to provide the correct intronic/exonic sequence of the BRCA2 gene.

It is another object of this invention to provide five unique haplotype sequences of the BRCA2 gene in normal individuals which do not correspond to increased cancer susceptibility.

It is another object of this invention to sequence a BRCA2 gene or a portion thereof and compare it to the five haplotype sequences to determine whether a sequence variation noted represents a polymorphism or a potentially harmful mutation.

It is another object of this invention to provide a list of the pairs which occur at each of ten polymorphic points in the BRCA2 gene.

It is another object of this invention to provide the rates of occurrence for the polymorphisms at codons 289, 372, 455, 743, 894, 991, 1132, 1269, 2414, and 2951 in the BRCA2 gene.

It is another object of this invention to provide a method wherein all exons of BRCA2 gene or parts thereof, are amplified with one or more oligonucleotide primers.

It is another object of this invention to provide a method of identifying a individual who carries no mutation(s) of the BRCA2 gene and is therefore at no increased risk or susceptibility to breast or ovarian cancer based on a finding that the individual does not carry an abnormal BRCA2 genes.

It is another object of this invention to provide a method of identifying a mutation in BRCA2 gene leading to predisposition or higher susceptibility to breast or ovarian cancer.

It is another object of this invention to provide five novel BRCA2 protein sequences derived from five BRCA2 haplotype sequences.

It is another object of the invention to encompass prokaryotic or eukaryotic host cells comprising an expression vector having a DNA sequence that encodes for all or a fragment of the five novel BRCA2 protein sequences, a BRCA2 polypeptide thereof, or a functional equivalent thereof.

It is another object of the invention to encompass an anti-BRCA2 protein antibody using all of fragments of the five novel BRCA2 protein

sequences, a BRCA2 polypeptide thereof or a functional equivalent thereof as an immunogen.

There is a need in the art for cDNA sequences of the BRCA2 gene and for the protein sequences of BRCA2 gene from normal individuals who are not at risk for increased susceptibility for cancer. In order to determine whether a sample from a patient suspected of containing a BRCA2 mutation actually has the mutation, the patient's BRCA2 DNA and/or amino acid sequence need to be compared to all known normal BRCA2 sequences. Failure to compare the sequence obtained to all naturally occurring normal sequences may result in reporting a sample as containing a potentially harmful mutation when it is a polymorphism without clinical significance.

A person skilled in the art of genetic susceptibility testing will find the present invention useful for:

- a) identifying individuals having a normal BRCA2 gene with no coding sequence mutations, who therefore cannot be said to have an increased genetic susceptibility to breast or ovarian cancer from their BRCA2 genes;
- b) avoiding misinterpretation of normal polymorphisms found in the BRCA2 gene;
- c) determining the presence of a previously unknown mutation in the BRCA2 gene;
- d) identifying a mutation in exon 11 of BRCA2 which indicates a predisposition or higher susceptibility to ovarian cancer than breast cancer (i.e., resides in the putative "ovarian cancer cluster" region);
- e) probing a human sample of the BRCA2 gene by allele to determine the presence or absence of either polymorphic alleles or mutations;
- f) performing gene therapy with the correct BRCA2 gene sequence.
- g) performing protein replacement therapy with the correct BRCA 2 protein sequence or a functional equivalent thereof.

### **BRIEF DESCRIPTION OF THE FIGURES**

5 **FIGURE 1** shows the GenBank genomic sequence of BRCA2 (Accession Number U43746). The lower case letters denote intronic sequences and the upper case letters denote exonic sequences. Incorrect exonic sequences at exons 5 and 16 are shown with boldface type.

10 **FIGURE 2** shows the corrected genomic sequence of BRCA2. The lower case letters denote intronic sequences and the upper case letters denote exonic sequences. Corrected intronic and exonic sequences at exons 5, 11 and 15 are shown with boldface type.

15 **FIGURE 3** shows the alternative alleles at polymorphic sites along a chromosome which can be represented as a unit or "haplotype" within a gene such as BRCA2. The haplotype that is in GenBank (GB) is shown with light shading. Five additional haplotypes are shown in **FIGURE 3** (encompassing the alternative alleles found at nucleotide sites 1093, 1342, 1593, 2457, 2908, 3199, 3624, 4035, 7470 and 9079). BRCA2<sup>(omi-1)</sup>, BRCA2<sup>(omi-2)</sup>, BRCA2<sup>(omi-3)</sup>, BRCA2<sup>(omi-4)</sup>, and BRCA2<sup>(omi-5)</sup> are represented with mixed dark and light shading (numbers 2, 4, 6, 8 and 10 from left to right). In total, 5 of 10 haplotypes along the BRCA2 gene are unique.

20

### **DETAILED DESCRIPTION OF THE INVENTION**

#### **DEFINITIONS**

The following definitions are provided for the purpose of understanding this invention.

25 "Breast and Ovarian cancer" is understood by those skilled in the art to include breast, ovarian and pancreatic cancer in women and also breast, prostate and pancreatic cancer in men. BRCA2 is associated with genetic susceptibility to breast, ovarian and pancreatic cancer. Therefore, claims in this document which recite breast and/or ovarian cancer refer to breast, ovarian, prostate, and pancreatic cancers in men and women.

30 "Coding sequence" refers to those portions of a gene which, taken together, code for a peptide (protein), or which nucleic acid itself has function.

"Protein" or "peptide" refers to a sequence of amino acids which has function.

"BRCA2<sup>(omi)</sup>" refers to the genomic BRCA2 sequence disclosed in Genbank (Accession Number U43746) wherein,

- 5 (1) a 10 bp stretch (5'-TTTATTTTAG-3') is intronic at 3' end of intron 4, rather than at the 5' end of exon 5; and  
(2) a 16 bp stretch (5'-GTGTTCTCATAAACAG-3') is exonic at the 3' end of exon 15, rather than at the 5' end of exon.

10 "BRCA2<sup>(omi 1-5)</sup>" refers to five unique DNA sequences of the BRCA2 gene and their introns (particularly the splice sites adjacent to the exons). These sequences were found by end to end sequencing of the BRCA2 gene from 5 individuals randomly drawn from the population and who were documented to have no family history of breast or ovarian cancer. The sequenced exons were found not to contain any truncating mutations. In all  
15 cases the change of a nucleic acid at a polymorphic site lead to a codon change and a change of amino acid from the previously published standard in GenBank (see TABLE III). In some cases the frequency of occurrence of a nucleic acid change was found to differ from the published frequency or was newly determined. These sequence variations are believed to be alleles  
20 whose haplotypes do not indicate an increased risk for cancer.

"Normal DNA sequence" also called "normal gene sequence" refers to a nucleic acid sequence, the nucleic acid of which are known to occur at their respective positions with high frequency in a population of individuals who carry the gene which codes for a normally functioning protein, or which  
25 itself has normal function.

"Normal Protein Sequence" refers to the protein sequence, the amino acids of which are known to occur with high frequency in a population of individuals who carry the gene which codes for a normally functioning protein.

30 "Normal Sequence" refers to the nucleic acid or protein sequence, the nucleic or amino acids of which are known to occur with high frequency in a population of individuals who carry the gene which codes for a normally functioning protein, or which nucleic acid itself has a normal function.

"Haplotype" refers to a series of specific alleles within a gene along a chromosome.

"Functional allele profile" refers a list of those alleles in the normal population which have the full function.

5 "Mutation" refers to a base change or a gain or loss of base pair(s) in a DNA sequence, which results in a DNA sequence coding for a non-functional protein or a protein with substantially reduced or altered function.

"Polymorphism" refers to a base change in a DNA sequence which is not associated with known pathology.

10 "Primer" refers to a sequence comprising about 15 or more nucleotides having a sequence complementary to the BRCA2 gene. Other primers which can be used for primer hybridization will be known or readily ascertainable to those skilled in the art.

"Substantially complementary to" refers to primer sequences which  
15 hybridize to the sequences provided under stringent conditions and/or sequences having sufficient homology with BRCA2 sequences, such that the allele specific oligonucleotide primers hybridize to the BRCA2 sequences to which they are complementary.

"Isolated nucleic acids" refers to nucleic acids substantially free of  
20 other nucleic acids, proteins, lipids, carbohydrates or other materials with which they may be associated. Such association is typically either in cellular material or in a synthesis medium.

"Biological sample" or "body sample" refers to a sample containing DNA obtained from a biological source. The sample may be from a living,  
25 dead or even archeological source from a variety of tissues and cells. Examples include body fluid (e.g. blood (leukocytes), urine (epithelial cells), saliva, breast milk, menstrual flow, cervical and vaginal secretions, etc.), skin, hair roots/follicle, mucus membrane (e.g. buccal or tongue cell scrapings), cervicovaginal cells (from PAP smear, etc.), lymphatic tissue, internal tissue  
30 (normal or tumor).

"Vector" refers to any polynucleotide which is capable of self replication or inducing integration into a self-replicating polynucleotide. Examples include polynucleotides containing an origin of replication or an

integration site. Vectors may be intergrated into the host cell's chromosome or form an autonomously replicating unit.

5 "A tumor growth inhibitor" refers to a molecule such as, all or a fragment of BRCA2 protein, a BRCA2 polypeptide, or a functional equivalent thereof that is effective for preventing the formation of, reducing, or eliminating a transformed or malignant phenotype of breast or ovarian cancer cells.

10 "A BRCA2 polypeptide" refers to a BRCA2 polypeptide either directly derived from the BRCA2 protein, or homologous to the BRCA2 protein, or a fusion protein consisting of all or fragments of the BRCA2 protein and polypeptides.

15 "A functional equivalent" refers to a molecule including an unnatural BRCA2 polypeptide, a drug or a natural product which retains substantial biological activity as the native BRCA2 protein. The activity and function of BRCA2 protein may include transactivation, granin, DNA repair, among others.

20 "A target polynucleotide" refers to the nucleic acid sequence of interest, for example, the BRCA2 encoding polynucleotide. Other primers which can be used for primer hybridization will be known or readily ascertainable to those of skill in the art.

25 The invention in several of its embodiments includes: an isolated DNA sequence of the BRCA2 coding sequence as set forth in SEQ ID NO:4, 6, 8, 10, and 12, a protein sequence of the BRCA2 protein as set forth in SEQ ID NO:5, 7, 9, 11, 13, a method of identifying individuals having a normal BRCA2 gene with no increased risk for breast and ovarian cancer, a method of detecting an increased genetic susceptibility to breast and ovarian cancer in an individual resulting from the presence of a mutation in the BRCA2 coding sequence, a method of performing gene therapy to prevent or treat a tumor, a method of protein replacement therapy to prevent or treat a tumor, a  
30 diagnostic reagent comprising all or fragments of the disclosed BRCA2 cDNA and protein sequences.

## SEQUENCING

Any nucleic acid specimen, in purified or non-purified form, can be utilized as the starting nucleic acid, providing it contains, or is suspected of containing, the specific nucleic acid sequence containing a polymorphic or a mutant allele. Thus, the process may amplify, for example, DNA or RNA, including mRNA and cDNA, wherein DNA or RNA may be single stranded or double stranded. In the event that RNA is to be used as a template, enzymes and/or conditions optimal for reverse transcribing the template to DNA would be utilized. In addition, a DNA-RNA hybrid which contains one strand of each may be utilized. A mixture of nucleic acids may also be employed, or the nucleic acids produced in a previous method such as an amplification reaction using the same or different primers may be so utilized. The specific nucleic acid sequence to be amplified, *i.e.*, the polymorphic and/or the mutant allele, may be a fraction of a larger molecule or can be present initially as a discrete molecule, so that the specific sequence constitutes the entire nucleic acid. A variety of amplification techniques may be used such as ligating the DNA sample or fragments thereof to a vector capable of replication or incorporation into a replicating system thereby increasing the number of copies of DNA suspected of containing at least a portion of the BRCA2 gene. Amplification techniques include so called "shot gun cloning". It is not necessary that the sequence to be amplified be present initially in a pure form; it may be a minor fraction of a complex mixture, such as contained in whole human DNA.

It should be noted that one need not sequence the entire coding region or even an entire DNA fragment in order to determine whether or not a mutation is present. For example, when a mutation is known in one family member, it is sufficient to determine the sequence at only the mutation site by sequencing or by other mutation detection systems such as ASO when testing other family members.

DNA utilized herein may be extracted from a body sample, such as blood, tissue material and other biological sample by a variety of techniques such as that described by Maniatis, *et al.* in *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor, NY, p 280-281, 1982). If the extracted sample is impure, it may be treated before amplification with an amount of a reagent



effective to open the cells, and to expose and/or separate the strand(s) of the nucleic acid(s). This lysing and nucleic acid denaturing step to expose and separate the strands will allow amplification to occur much more readily.

For amplification by cloning, the isolated DNA may be cleaved into  
5 fragments by a restriction endonuclease or by shearing by passing the DNA containing mixture through a 25 gauge needle from a syringe to prepare 1-1.5 kb fragments. The fragments are then ligated to a cleaved vector (virus, plasmid, transposon, cosmid etc.) and then the recombinant vector so formed is then replicated in a manner typical for that vector.

10 For a PCR amplification, the deoxyribonucleotide triphosphates dATP, dCTP, dGTP, and dTTP are added to the synthesis mixture, either separately or together with the primers, in adequate amounts and the resulting solution is heated to about 90°-100°C from about 1 to 10 minutes, preferably from 1 to 4 minutes. After this heating period, the solution is  
15 allowed to cool, which is preferable for the primer hybridization. To the cooled mixture is added an appropriate agent for effecting the primer extension reaction (called herein "agent for polymerization"), and the reaction is allowed to occur under conditions known in the art. The agent for polymerization may also be added together with the other reagents if it is  
20 heat stable. This synthesis (or amplification) reaction may occur at room temperature up to a temperature above which the agent for polymerization no longer functions. Thus, for example, if DNA polymerase is used as the agent, the temperature is generally no greater than about 40°C. Most conveniently the reaction occurs at room temperature. When using  
25 thermostable DNA polymerase such as Taq, higher temperature may be used.

The allele specific oligonucleotide primers are useful in determining whether a subject is at risk of having breast or ovarian cancer, and also useful for characterizing a tumor. Primers direct amplification of a target  
30 polynucleotide prior to sequencing. These unique BRCA2 oligonucleotide primers for exons 2-27 shown in TABLE II were designed and produced specifically to optimize amplification of portions of BRCA2 which are to be sequenced.

The primers used to carry out this invention embrace oligonucleotides of sufficient length and appropriate sequence to provide initiation of polymerization. Environmental conditions conducive to synthesis include the presence of nucleoside triphosphates and an agent for polymerization, such as DNA polymerase, and a suitable temperature and pH. The primer is preferably single stranded for maximum efficiency in amplification, but may be double stranded. If double stranded, the primer is first treated to separate its strands before being used to prepare extension products. The primer must be sufficiently long to prime the synthesis of extension products in the presence of the inducing agent for polymerization. The exact length of primer will depend on many factors, including temperature, buffer, and nucleotide composition. The oligonucleotide primer typically contains 18-28 bp plus in some cases an M13 "tail" for convenience.

Primers used to carry out this invention are designed to be substantially complementary to each strand of the genomic locus to be amplified. This means that the primers must be sufficiently complementary to hybridize with their respective strands under conditions which allow the agent for polymerization to perform. In other words, the primers should have sufficient complementarity with the 5' and 3' sequences flanking the mutation to hybridize therewith and permit amplification of the genomic locus.

Oligonucleotide primers of the invention are employed in the amplification process which is an enzymatic chain reaction that produces exponential quantities of polymorphic locus relative to the number of reaction steps involved. Typically, one primer is complementary to the negative (-) strand of the polymorphic locus and the other is complementary to the positive (+) strand. Annealing the primers to denatured nucleic acid followed by extension with an enzyme, such as the large fragment of DNA polymerase I (Klenow) and nucleotides, results in newly synthesized + and - strands containing the target polymorphic locus sequence. Because these newly synthesized sequences are also templates, repeated cycles of denaturing, primer annealing, and extension results in exponential production of the region (*i.e.*, the target polymorphic locus sequence) defined by the primers. The product of the chain reaction is a discrete nucleic acid

duplex with termini corresponding to the ends of the specific primers employed.

The oligonucleotide primers of the invention may be prepared using any suitable method, such as conventional phosphotriester and phosphodiester methods or automated embodiments thereof. In one such automated embodiment, diethylphosphoramidites are used as starting materials and may be synthesized as described by Beaucage, *et al.*, *Tetrahedron Letters*, 22:1859-1862, 1981. One method for synthesizing oligonucleotides on a modified solid support is described in U.S. Patent No. 4,458,066.

The agent for polymerization may be any compound or system which will function to accomplish the synthesis of primer extension products, including enzymes. Suitable enzymes for this purpose include, for example, *E. coli* DNA polymerase I, Klenow fragment of *E. coli* DNA polymerase, polymerase muteins, reverse transcriptase, other enzymes, including heat-stable enzymes (*i.e.*, those enzymes which perform primer extension after being subjected to temperatures sufficiently elevated to cause denaturation), such as *Taq* polymerase. Suitable enzymes will facilitate combination of the nucleotides in the proper manner to form the primer extension products which are complementary to each polymorphic locus nucleic acid strand. Generally, the synthesis will be initiated at the 3' end of each primer and proceed in the 5' direction along the template strand, until synthesis terminates, producing molecules of different lengths.

The newly synthesized strand and its complementary nucleic acid strand will form a double-stranded molecule under hybridizing conditions described above and this hybrid is used in subsequent steps of the process. In the next step, the newly synthesized double-stranded molecule is subjected to denaturing conditions using any of the procedures described above to provide single-stranded molecules.

The steps of denaturing, annealing, and extension product synthesis can be repeated as often as needed to amplify the target polymorphic locus nucleic acid sequence to the extent necessary for detection. The amount of the specific nucleic acid sequence produced will accumulate in an

exponential fashion. Amplification is described in *PCR. A Practical Approach*, ILR Press, Eds. M. J. McPherson, P. Quirke, and G. R. Taylor, 1992.

5 The amplification products may be detected by Southern blots analysis, without using radioactive probes. In such a process, for example, a small sample of DNA containing a very low level of the nucleic acid sequence of the polymorphic locus is amplified, and analyzed via a Southern blotting technique or similarly, using dot blot analysis. The use of non-radioactive probes or labels is facilitated by the high level of the amplified  
10 signal. Alternatively, probes used to detect the amplified products can be directly or indirectly detectably labeled, for example, with a radioisotope, a fluorescent compound, a bioluminescent compound, a chemiluminescent compound, a metal chelator or an enzyme. Those of ordinary skill in the art will know of other suitable labels for binding to the probe, or will be able to  
15 ascertain such, using routine experimentation.

Sequences amplified by the methods of the invention can be further evaluated, detected, cloned, sequenced, and the like, either in solution or after binding to a solid support, by any method usually applied to the detection of a specific DNA sequence such as PCR, oligomer restriction  
20 (Saiki, *et al.*, *Bio/Technology*, 3:1008-1012, 1985), allele-specific oligonucleotide (ASO) probe analysis (Conner, *et al.*, *Proc. Natl. Acad. Sci. U.S.A.*, 80:278, 1983), oligonucleotide ligation assays (OLAs) (Landgren, *et al.*, *Science*, 241:1007, 1988), and the like. Molecular techniques for DNA analysis have been reviewed (Landgren, *et al.*, *Science*, 242:229-237,  
25 1988).

Preferably, the method of amplifying is by PCR, as described herein and as is commonly used by those of ordinary skill in the art. Alternative methods of amplification have been described and can also be employed as long as the BRCA2 locus amplified by PCR using primers of the invention is  
30 similarly amplified by the alternative means. Such alternative amplification systems include but are not limited to self-sustained sequence replication, which begins with a short sequence of RNA of interest and a T7 promoter. Reverse transcriptase copies the RNA into cDNA and degrades the RNA,

followed by reverse transcriptase polymerizing a second strand of DNA.

Another nucleic acid amplification technique is nucleic acid sequence-based amplification (NASBA) which uses reverse transcription and T7 RNA polymerase and incorporates two primers to target its cycling scheme.

- 5 NASBA can begin with either DNA or RNA and finish with either, and amplifies to  $10^8$  copies within 60 to 90 minutes. Alternatively, nucleic acid can be amplified by ligation activated transcription (LAT). LAT works from a single-stranded template with a single primer that is partially single-stranded and partially double-stranded. Amplification is initiated by ligating a cDNA to
- 10 the promoter oligonucleotide and within a few hours, and amplification is  $10^8$  to  $10^9$  fold. Another amplification system useful in the method of the invention is the Q $\beta$  Replicase System. The Q $\beta$  replicase system can be utilized by attaching an RNA sequence called MDV-1 to RNA complementary to a DNA sequence of interest. Upon mixing with a sample, the hybrid RNA
- 15 finds its complement among the specimen's mRNAs and binds, activating the replicase to copy the tag-along sequence of interest. Another nucleic acid amplification technique, ligase chain reaction (LCR), works by using two differently labeled halves of a sequence of interest which are covalently bonded by ligase in the presence of the contiguous sequence in a sample,
- 20 forming a new target. The repair chain reaction (RCR) nucleic acid amplification technique uses two complementary and target-specific oligonucleotide probe pairs, thermostable polymerase and ligase, and DNA nucleotides to geometrically amplify targeted sequences. A 2-base gap separates the oligonucleotide probe pairs, and the RCR fills and joins the
- 25 gap, mimicking normal DNA repair. Nucleic acid amplification by strand displacement activation (SDA) utilizes a short primer containing a recognition site for *hincII* with short overhang on the 5' end which binds to target DNA. A DNA polymerase fills in the part of the primer opposite the overhang with sulfur-containing adenine analogs. *HincII* is added but only cuts the
- 30 unmodified DNA strand. A DNA polymerase that lacks 5' exonuclease activity enters at the site of the nick and begins to polymerize, displacing the initial primer strand downstream and building a new one which serves as

more primer. SDA produces greater than  $10^7$ -fold amplification in 2 hours at 37°C. Unlike PCR and LCR, SDA does not require instrumented Temperature cycling.

Another method is a process for amplifying nucleic acid sequences from a DNA or RNA template which may be purified or may exist in a mixture of nucleic acids. The resulting nucleic acid sequences may be exact copies of the template, or may be modified. The process has advantages over PCR in that it increases the fidelity of copying a specific nucleic acid sequence, and it allows one to more efficiently detect a particular point mutation in a single assay. A target nucleic acid is amplified enzymatically while avoiding strand displacement. Three primers are used. A first primer is complementary to the first end of the target. A second primer is complementary to the second end of the target. A third primer which is similar to the first end of the target and which is substantially complementary to at least a portion of the first primer such that when the third primer is hybridized to the first primer, the position of the third primer complementary to the base at the 5' end of the first primer contains a modification which substantially avoids strand displacement. This method is detailed in U.S. Patent 5,593,840 to Bhatnagar et al. 1997, incorporated herein by reference.

Finally, recent application of DNA chips or microarray technology where DNA or oligonucleotides are immobilized on small solid support may also be used to rapidly sequence sample BRCA2 gene and analyze its expression. Typically, high density arrays of DNA fragment are fabricated on glass or nylon substrates by *in situ* light-directed combinatorial synthesis or by conventional synthesis followed by immobilization (Fodor *et al.* U.S. patent No. 5,445,934). Sample DNA or RNA may be amplified by PCR, labeled with a fluorescent tag, and hybridized to the microarray. Examples of this technology are provided in U.S. Patents 5,510, 270, U.S. 5,547,839, incorporated herein by reference.

All exonic and adjacent intronic sequences of the BRCA2 gene were obtained by end to end sequencing of five normal subjects in the manner described above followed by analysis of the data obtained. The data obtained provided us with the opportunity to establish the correct

intronic/exonic structure of the BRCA2 gene. In addition, we evaluated six previously published normal polymorphisms (1342, 2457, 3199, 3624, 4035, and 7470) for correctness and frequency in the population, and to identify four additional polymorphisms not previously characterized (1093, 1593, 2908, and 9079).

## GENE THERAPY

The polynucleotide(s) which result from either sense or antisense transcription of any exon or the entire coding sequence or fragments of BRCA2 gene may be used for gene therapy. A variety of methods are known for gene transfer, any of which might be available for use.

### Direct injection of Recombinant DNA in vivo:

1. Direct injection of "naked" DNA directly with a syringe and needle into a specific tissue, infused through a vascular bed, or transferred through a catheter into endothelial cells.
2. Direct injection of DNA that is contained in artificially generated lipid vesicles or other encapsulating vehicles.
3. Direct injection of DNA conjugated to a target receptor structure, such as a diphtheria toxin, an antibody or other suitable receptor.
4. Direct injection by particle bombardment. For example, the DNA may be coated onto gold particles and shot into the cells.

### Human Artificial Chromosomes

The gene delivery approach involves the use of human chromosomes that have been stripped down to contain only the essential components for replication and the genes desired for transfer.

### Receptor-Mediated Gene Transfer

DNA is linked to a targeting molecule that will bind to specific cell-surface receptors, inducing endocytosis and transfer of the DNA into mammalian cells. One such technique uses poly-L-lysine to link asialoglycoprotein to DNA. An adenovirus is also added to the complex to disrupt the lysosomes and thus allow the DNA to avoid degradation and move to the nucleus. Infusion of these particles intravenously has resulted in gene transfer into hepatocytes.

## RECOMBINANT VIRUS VECTORS

Several vectors may be used in gene therapy. Among them are the Moloney Murine Leukemia Virus (MoMLV) Vectors, the adenovirus vectors, the Adeno-Associated Virus (AAV) vectors, the herpes simplex virus (HSV) vectors, the poxvirus vectors, the retrovirus vectors, and human immunodeficiency virus (HIV) vectors.

## GENE REPLACEMENT AND REPAIR

The ideal genetic manipulation for treatment of a genetic disease would be the actual replacement of the defective gene with a normal copy of the gene. Homologous recombination is the term used for switching out a section of DNA and replacing it with a new piece. By this technique, the defective gene may be replaced with a normal gene which expresses a functioning BRCA2 tumor growth inhibitor protein.

A complete description of gene therapy can also be found in "Gene Therapy A Primer For Physicians" 2d Ed. by Kenneth W. Culver, M.D. Publ. Mary Ann Liebert Inc. (1996). Two Gene Therapy Protocols for BRCA1 gene have been approved by the Recombinant DNA Advisory Committee for Jeffrey T. Holt et al. They are listed as 9602-148, and 9603-149 and are available from the NIH. Protocols for BRCA2 gene therapy may be similarly employed. The isolated BRCA2 gene may be synthesized or constructed from amplification products and inserted into a vector such as the LXS vector.

## A BRCA2 POLYPEPTIDE OR ITS FUNCTIONAL EQUIVALENT

The growth of breast and ovarian cancer may be arrested or prevented by directly increasing the BRCA2 protein level where inadequate functional BRCA2 activity is responsible for breast and ovarian cancer. The cDNA and amino acid sequences of five novel BRCA2 haplotypes are disclosed herein (SEQ ID No:4-13). All or a fragment of BRCA2 protein may be used in therapeutic or prophylactic treatment of breast and ovarian cancer. Such a fragment may have a similar biological function as the native BRCA2 protein



or may have a desired biological function as specified below. BRCA2 polypeptides or their functional equivalents including homologous and modified polypeptide sequences are also within the scope of the present invention. Changes in the native sequence may be advantageous in  
5 producing or using the BRCA2 derived polypeptides or functional equivalents suitable for therapeutic or prophylactic treatment of breast and ovarian cancer. For example, these changes may be desirable for producing resistance against *in vivo* proteolytic cleavage, for facilitating transportation and delivery of therapeutic reagents, for localizing and compartmentalizing tumor  
10 suppressing agents, or for expression, isolating and purifying the target species.

There are a variety of methods to produce an active BRCA2 polypeptide or a functional equivalent as a tumor growth inhibitor. For example, one or more amino acids may be substituted, deleted, or inserted  
15 using methods well known in the art (Maniatis *et al.*, 1982). Considerations of polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphiphathic nature of the amino acids play an important role in designing homologous polypeptide changes suitable for the intended treatment. In particular, conservative amino acid substitution using amino acids that are  
20 related in side-chain structure and charge may be employed to preserve the chemical and biological property. A homologous polypeptide typically contains at least 70% homology to the native sequence. Unnatural forms of the polypeptide may also be incorporated so long as the modification retains substantial biological activity. These unnatural polypeptides typically include  
25 structural mimics and chemical medications, which have similar three-dimensional structures as the active regions of the native BRCA2 protein. For example, these modifications may include terminal D-amino acids, cyclic peptides, unnatural amino acids side chains, pseudopeptide bonds, N-terminal acetylation, glycosylation, and biotinylation, etc. These unnatural  
30 forms of polypeptide may have a desired biological function, for example, they may be particularly robust in the presence of cellular or serum proteases and exopeptidase. An effective BRCA2 polypeptide or a functional equivalent may also be recognized by the reduction of the native

BRCA2 protein. Regions of the BRCA2 protein may be systematically deleted to identify which regions are essential for tumor growth inhibitor activity. These smaller fragments of BRCA2 protein may then be subjected to structural and functional modification to derive therapeutically or prophylactically effective regiments. Finally, drugs, natural products or small molecules may be screened or synthesized to mimic the function of the BRCA2 protein. Typically, the active species retain the essential three-dimensional shape and chemical reactivity, and therefore retain the desired aspects of the biological activity of the native BRCA2 protein. The activity and function of BRCA2 may include transactivation, granin, DNA repair among others. Functions of BRCA2 protein are also reviewed in Bertwistle and Ashworth, *Curr. Opin. Genet. Dev.* 8(1): 14-20 (1998) and Zhang *et al.*, *Cell* 92:433-436 (1998). It will be apparent to one skilled in the art that a BRCA2 polypeptide or a functional equivalent may be selected because such polypeptide or functional equivalent possesses similar biological activity as the native BRCA2 protein.

#### EXPRESSION OF THE BRCA2 PROTEIN AND POLYPEPTIDE IN HOST CELLS

All or fragments of the BRCA2 protein and polypeptide may be produced by host cells that are capable of directing the replication and the expression of foreign genes. Suitable host cells include prokaryotes, yeast cells, or higher eukaryotic cells, which contain an expression vector comprising all or a fragment of the BRCA2 cDNA sequence (SEQ. ID No: 4, 6, 8, 10, or 12) operatively linked to one or more regulatory sequences to produce the intended BRCA2 protein or polypeptide. Prokaryotes may include gram negative or gram positive organisms, for example *E. coli* or *Bacillus* strains. Suitable eukaryotic host cells may include yeast, virus, and mamalian systems. For example, Sf9 insect cells and human cell lines, such as COS, MCF7, HeLa, 293T, HBL100, SW480, and HCT116 cells.

A broad variety of suitable expression vectors are available in the art. An expression vector typically contains an origin of replication, a promoter, a phenotypic selection gene (antibiotic resistance or autotrophic requirement),

and a DNA sequence coding for all or fragments of the BRCA2 protein. The expression vectors may also include other operatively linked regulatory DNA sequences known in the art, for example, stability leader sequences, secretory leader sequences, restriction enzyme cleavage sequences, polyadenylation sequences, and termination sequences, among others. The essential and regulatory elements of the expression vector must be compatible with the intended host cell. Suitable expression vectors containing the desired coding and control regions may be constructed using standard recombinant DNA techniques known in the art, many of which are described in Sambrook, *et al.*, Molecular Cloning: A Laboratory Manual, Second Edition, Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y. (1989). For example, suitable origins of replication may include Col E1, SV40 viral and M13 origins of replication. Suitable promoters may be constitutive or inducible, for example, tac promoter, lac Z promoter, SV40 promoter, MMTV promoter, and LXSX promoter. Examples of selectable markers include neomycin, ampicillin, and hygromycin resistance and the like. Many suitable prokaryotic, viral and mammalian expression vectors may be obtained commercially, for example, from Invitrogen Corp., San Diego, CA or from Clontech, Palo Alto, CA. It may be desirable that the BRCA2 protein or polypeptide is produced as a fusion protein to enhance the expression in selected host cells, to detect the expression in transfected cells, or to simplify the purification process. Suitable fusion partners for the BRCA2 protein or polypeptide are well known in the art and may include  $\beta$ -galactosidase, glutathione-S-transferase, and poly-histidine tag.

Expression vectors may be introduced into host cells by various methods known in the art. The transformation procedure used depends upon the host to be transformed. Methods for introduction of vectors into host cells may include calcium phosphate precipitation, electroporation, dextran-mediated transfection, liposome encapsulation, nucleus microinjection, and viral or phage infection, among others.

Once an expression vector has been introduced into a suitable host cell, the host cell may be cultured under conditions permitting expression of large amounts of the BRCA2 protein or polypeptide. The expression product

may be identified by many approaches well known in the art, for example, sequencing after PCR-based amplification, hybridization using probes complementary to the desired DNA sequence, the presence or absence of marker gene functions such as enzyme activity or antibiotic resistance, the level of mRNA production encoding the intended sequence, immunological  
5 detection of a gene product using monoclonal and polyclonal antibodies, such as Western blotting or ELISA. The BRCA2 protein or polypeptides produced in this manner may then be isolated following cell lysis and purified using various protein purification techniques known in the art, for example, ion  
10 exchange chromatography, gel filtration chromatography and immunoaffinity chromatography.

It is generally preferred that whenever possible, longer fragments of BRCA2 protein or polypeptide are used, particularly to include the desired functional domains of BRCA2 protein. Expression of shorter fragments of  
15 DNA may be useful in generating BRCA2 derived immunogen for the production of anti-BRCA2 antibodies. It should, of course, be understood that not all expression vectors, DNA regulatory sequences or host cells will function equally well to express the BRCA2 protein or polypeptides of the present invention. However, one of ordinary skill in the art may make a  
20 selection among expression vectors, DNA regulatory sequences, host cells, and codon usage in order to optimize expression using known technology in the art without undue experimentation. Studies of BRCA2 protein function and examples of genetic manipulation of BRCA2 protein are summarized in two recent review articles, Bertwistle and Ashworth, *Curr. Opin. Genet. Dev.*  
25 8(1): 14-20 (1998) and Zhang *et al.*, *Cell* 92:433-436 (1998).

#### IN VITRO SYNTHESIS AND CHEMICAL SYNTHESIS

Although it is preferred that fragments of the BRCA2 protein or polypeptides be obtained by overexpression in prokaryotic or eukaryotic host  
30 cells, the BRCA2 polypeptides or their functional equivalents may also be obtained by *in vitro* translation or synthetic means by methods known to those of ordinary skill in the art. For example, *in vitro* translation may employ an mRNA encoded by a DNA sequence coding for fragments of the BRCA2

protein or polypeptides. Chemical synthesis methodology such as solid phase synthesis may be used to synthesize a BRCA2 polypeptide structural mimic and chemically modified analogs thereof. The polypeptides or the modifications and mimic thereof produced in this manner may then be  
5 isolated and purified using various purification techniques, such as chromatographic procedures including ion exchange chromatography, gel filtration chromatography and immunoaffinity chromatography.

#### PROTEIN REPLACEMENT THERAPY

10 The tumor suppressing function of BRCA2 suggests that various BRCA2 protein targeted therapies may be utilized in treating and preventing tumors in breast and ovarian cancer. The present invention therefore includes therapeutic and prophylactic treatment of breast and ovarian cancer using therapeutic pharmaceutical compositions containing the BRCA2  
15 protein, polypeptides, or their functional equivalents. For example, protein replacement therapy may involve directly administering the BRCA2 protein, a BRCA2 polypeptide, or a functional equivalent in a pharmaceutically effective carrier. Alternatively, protein replacement therapy may utilize tumor antigen specific antibody fused to fragments of the BRCA2 protein, a polypeptide, or  
20 a functional equivalent to deliver anti-cancer regiments specifically to the tumor cells.

To prepare the pharmaceutical compositions of the present invention, an active BRCA2 protein, a BRCA2 polypeptide, or its functional equivalent is combined with a pharmaceutical carrier selected and prepared according to  
25 conventional pharmaceutical compounding techniques. A suitable amount of the composition may be administered locally to the site of a tumor or systemically to arrest the proliferation of tumor cells. The methods for administration, may include parenteral, oral, or intravenous, among others according to established protocols in the art.

30 Pharmaceutically acceptable solid or liquid carriers or components which may be added to enhance or stabilize the composition, or to facilitate preparation of the composition include, without limitation, syrup, water, isotonic solution, 5 % glucose in water or buffered sodium or ammonium

acetate solution, oils, glycerin, alcohols, flavoring agents, preservatives, coloring agents, starches, sugars, diluents, granulating agents, lubricants, binders, and sustained release materials. The dosage at which the therapeutic compositions are administered may vary within a wide range and depends on various factors, such as the stage of cancer progression, the age and condition of the patient, and may be individually adjusted.

#### DIAGNOSTIC REAGENTS

The BRCA2 protein, polypeptides, their functional equivalents, antibodies, and polynucleotides may be used in a wide variety of ways in addition to gene therapy and protein replacement therapy. They may be useful as diagnostic reagents to measure normal or abnormal activity of BRCA2 at the DNA, RNA, and protein level. The present invention therefore encompasses the diagnostic reagents derived from the BRCA2 cDNA and protein sequences as set forth in SEQ. ID. Nos: 4-13. These reagents may be utilized in methods for monitoring disease progression, for determining patients suited for gene and protein replacement therapy, or for detecting the presence or quantifying the amount of a tumor growth inhibitor following such therapy. Such methods may involve conventional histochemical techniques, such as obtaining a tumor tissue from the patient, preparing an extract and testing this extract for tumor growth or metabolism. For example, the test for tumor growth may involve measuring abnormal BRCA2 activity using conventional diagnostic assays, such as Southern, Northern, and Western blotting, PCR, RT-PCR, and immunoprecipitation. In biopsies of tumor tissues, the loss of BRCA2 expression in tumor tissue may be verified by RT-PCR and Northern blotting at the RNA level. A Southern blot analysis, genomic PCR, or fluorescence in situ hybridization (FISH) may also be performed to examine the mutations of BRCA2 at the DNA level. And, a Western blotting, protein truncation assay, or immunoprecipitation may be utilized to analysis the effect at the protein level.

These diagnostic reagents are typically either covalently or non covalently attached to a detectable label. Such a label includes a radioactive label, a colorimetric enzyme label, a fluorescence label, or an

epitope label. Frequently, a reporter gene downstream of the regulatory sequences is fused with the BRCA2 protein or polypeptide to facilitate the detection and purification of the target species. Commonly used reporter genes in BRCA2 fusion proteins include  $\beta$ -galactosidase and luciferase gene.

5 The BRCA2 protein, polypeptides, their functional equivalents, antibodies, and polynucleotides may also be useful in the study of the characteristics of BRCA2 proteins, such as structure and function of BRCA2 in oncogenesis or subcellular localization of BRCA2 protein in normal and cancerous cell. For example, yeast two-hybrid system has been used in the study of cellular function of BRCA2 to identify the regulator and effector of BRCA2 tumor suppressing function (Sharan *et al.*, *Nature* 386:804-810 (1997) and Katagiri *et al.*, *Genes, Chromosomes & Cancer* 21:217-222 (1988)). In addition, the BRCA2 protein, polypeptides, their functional  
10 equivalents, antibodies, and polynucleotides may also be used in *in vivo* cell based and *in vitro* cell free assays to screen natural products and synthetic compounds which may mimic, regulate or stimulate BRCA2 protein function.  
15

#### ANTISENSE INHIBITION

20 Antisense suppression of endogenous BRCA2 expression may assess the effect of BRCA2 protein on cell growth inhibition using known method in the art (Crooke, *Annu. Rev. Pharmacol. Toxicol.* 32:329-376 (1992) and Robinson-Benion and Holt, *Methods Enzymol.* 254:363-375 (1995)). Given the cDNA sequence as set forth in SEQ ID. NO: 4, 6, 8, 10, and 12, one of  
25 skill in the art can readily obtain anti-sense strand of DNA and RNA sequences to interfere with the production of wild-type BRCA2 protein or the mutated form of BRCA2 protein. Alternatively, antisense oligonucleotide may be designed to target the control sequences of BRCA2 gene to reduce or prevent the expression of the endogenous BRCA2 gene.  
30

#### ANTIBODIES

The BRCA2 protein, polypeptides, or their functional equivalents may be used as immunogens to prepare polyclonal or monoclonal antibodies

capable of binding the BRCA2 derived antigens in a known manner (Harlow & Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, 1988). These antibodies may be used for the detection of the BRCA2 protein, polypeptides, or a functional equivalent in an immunoassay, such as ELISA, Western blot, radioimmunoassay, enzyme immunoassay, and immunocytochemistry. Typically, an anti-BRCA2 antibody is in solution or is attached to a solid surface such as a plate, a particle, a bead, or a tube. The antibody is allowed to contact a biological sample or a blot suspected of containing the BRCA2 protein or polypeptide to form a primary immunocomplex. After sufficient incubation period, the primary immunocomplex is washed to remove any non-specifically bound species. The amount of specifically bound BRCA2 protein or polypeptide may be determined using the detection of an attached label or a marker, such as a radioactive, a fluorescent, or an enzymatic label. Alternatively, the detection of BRCA2 derived antigen is allowed by forming a secondary immunocomplex using a second antibody which is attached with a such label or marker. The antibodies may also be used in affinity chromatography for isolating or purifying the BRCA2 protein, polypeptides or their functional equivalents.

20

### **EXAMPLE 1**

#### **Determination of the Coding Sequence Haplotypes of the BRCA2 Gene From Normal Individuals**

Approximately 150 volunteers were screened in order to identify individuals with no cancer history in their immediate family (i.e. first and second degree relatives). Each person was asked to fill out a hereditary cancer prescreening questionnaire (See TABLE I). Five of these were randomly chosen for end-to-end sequencing of their BRCA2 gene. A first degree relative is a parent, sibling, or offspring. A second degree relative is an aunt, uncle, grandparent, grandchild, niece, nephew, or half-sibling.

30

Genomic DNA was isolated from white blood cells of five normal subjects selected from analysis of their answers to the questions above.



Dideoxy sequence analysis was performed following polymerase chain reaction amplification.

All exons of the BRCA2 gene were subjected to direct dideoxy sequence analysis by asymmetric amplification using the polymerase chain reaction (PCR) to generate a single stranded product amplified from this DNA sample. Shuldiner, *et al.*, *Handbook of Techniques in Endocrine Research*, p. 457-486, DePablo, F., Scanes, C., eds., Academic Press, Inc., 1993. Fluorescent dye was attached for automated sequencing using the Taq Dye Terminator Kit (Perkin-Elmer® cat# 401628). DNA sequencing was performed in both forward and reverse directions on an Applied Biosystems, Inc. (ABI) automated sequencer (Model 377). The software used for analysis of the resulting data was "Sequence Navigator" purchased through ABI.

1. Polymerase Chain Reaction (PCR) Amplification

Genomic DNA (100 nanograms) extracted from white blood cells of five normal subjects. Each of the five samples was sequenced end to end. Each sample was amplified in a final volume of 25 microliters containing 1 microliter (100 nanograms) genomic DNA, 2.5 microliters 10X PCR buffer (100 mM Tris, pH 8.3, 500 mM KCl, 1.2 mM MgCl<sub>2</sub>), 2.5 microliters 10X dNTP mix (2 mM each nucleotide), 2.5 microliters forward primer, 2.5 microliters reverse primer, and 1 microliter Taq polymerase (5 units), and 13 microliters of water.

The primers in TABLE II below were used to carry out amplification of the various sections of the BRCA2 gene samples. The primers were synthesized on an DNA/RNA Synthesizer Model 394®.

Thirty-five cycles were performed, each consisting of denaturing (95°C; 30 seconds), annealing (55°C; 1 minute), and extension (72°C; 90 seconds), except during the first cycle in which the denaturing time was increased to 5 minutes, and during the last cycle in which the extension time was increased to 5 minutes.

PCR products were purified using Qia-quick<sup>®</sup> PCR purification kits (Qiagen<sup>®</sup>, cat# 28104; Chatsworth, CA). Yield and purity of the PCR product are determined spectrophotometrically at OD<sub>260</sub> on a Beckman DU 650 spectrophotometer.

5

## 2. Dideoxy Sequence Analysis

Fluorescent dye was attached to PCR products for automated sequencing using the Taq Dye Terminator Kit (Perkin-Elmer<sup>®</sup> cat # 401628). DNA sequencing was performed in both forward and reverse directions on an Applied Biosystems, Inc. (ABI) Foster City, CA., automated sequencer (Model 377). The software used for analysis of the resulting data was "Sequence Navigator<sup>®</sup>" purchased through ABI.

10

## 3. RESULTS

Based upon the sequencing of the five normal individuals, it was determined that the standard sequence found in both GenBank and BIC were inaccurate. In Genbank, a 10 bp stretch (5'-TTTATTTTAG-3') was mistakenly listed as exonic at the 5' end of exon 5 while it should be intronic which would not be included in the cDNA and resultant protein. In addition, a more detrimental error that has the significant potential to lead to an incorrect diagnosis of breast cancer propensity exists in both Genbank and BIC: a sequence of 16 bp (5'-GTGTTCTCATAAACAG-3') should be at the end of exon 15, but instead is listed at the beginning of exon 16 in the database. The disclosure and listing of GenBank is shown in Figure 1. The correct intron/exon sequence of BRCA2 is presented in Figure 2, wherein,

15

20

25

(1) a 10 bp stretch (5'-TTTATTTTAG-3') is intronic at 3' end of intron 4, rather than at the 5' end of exon 5 (corrected exon 5 is listed as SEQ. ID. NO: 1) and

30

(2) a 16 bp stretch (5'-GTGTTCTCATAAACAG-3') is exonic at the 3' end of exon 15, rather than at the 5' end of exon 16 (corrected exons 15 and 16 are listed as SEQ. ID. No: 2 and 3 respectively)

The BIC BRCA2 sequence also contains sequence errors in which a stretch of nine nucleotides at positions 5554-5460 is listed as CGTTTGTGT (amino acids: Arg-Leu-Cys). The correct sequence at these positions is GTTTGTGTT (amino acids: Val-Cys-Val). In addition, the BIC BRCA2  
5 nucleotides at positions 2024 (codon 599), 4553 (codon 1442), 4815 (codon 1529), 5841 (codon 1871), and 5972 (codon 1915) are T, T, A, C, and T respectively, wherein the correct nucleotides at these positions are C, C, G, T, and C respectively. Among them, the nucleotide errors at codon 599, 1442, 1915 result in amino acids changes.

10 Additional differences in the nucleic acids of the five normal individuals were found in ten polymorphic locations. The changes and their positions are found in TABLE III. The individual haplotypes of each chromosome of BRCA2 are displayed in FIGURE 3. In each case, the initial haplotype reported in Genbank (accession number U43746) was subtracted to  
15 determine the new haplotypes OMI 1-5. Thus, the Genbank sequence only represents 50% of the haplotypes found; the five new BRCA2<sup>(omi 1-5)</sup> DNA sequences are shown as SEQ. ID. NO: 4, 6, 8, 10, and 12, respectively (See FIGURE 3), and the corresponding polypeptides are listed as SEQ. ID. NO: 5, 7, 9, 11, and 13 respectively. In combination, these seven haplotypes  
20 represent a functional allele profile for the BRCA2 gene.

The data show that for each of the samples, all exons of BRCA2 were identical except in the region of ten polymorphisms. Six of these polymorphisms were previously identified (Tartigan *et al.*, *Nature Genetics* 12: 333-337 (1996); Phelan *et al.*, *Nature Genetics* 13: 120-122 (1996); Couch  
25 *et al.*, *Nature Genetics* 13: 123-125 (1996); Teng, *et al.*, *Nature Genetics* 13: 241-244 (1996); Schubert *et al* 60: 1031-1040 (1997)), but four were unique to this work. Even though the individual polymorphisms may have been identified, none of these complete haplotypes has been previously determined.

**TABLE I**  
**Hereditary Cancer Pre-Screening Questionnaire**

**Part A: Answer the following questions about your family**

- 5 1. To your knowledge, has anyone in your family been diagnosed with a very specific hereditary colon disease called Familial Adenomatous Polyposis (FAP)?
- 10 2. To your knowledge, have you or any aunt had breast cancer diagnosed before the age 35?
3. Have you had Inflammatory Bowel Disease, also called Crohn's Disease or Ulcerative Colitis, for more than 7 years?

15 **Part B: Refer to the list of cancers below for your responses only to questions in Part B**

- |    |                    |                    |                   |
|----|--------------------|--------------------|-------------------|
|    | Bladder Cancer     | Lung Cancer        | Pancreatic Cancer |
|    | Breast Cancer      | Gastric Cancer     | Prostate Cancer   |
|    | Colon Cancer       | Malignant Melanoma | Renal Cancer      |
| 20 | Endometrial Cancer | Ovarian Cancer     | Thyroid Cancer    |
4. Have your mother or father, your sisters or brothers or your children had any of the listed cancers?
- 25 5. Have there been diagnosed in your mother's brothers or sisters, or your mother's parents more than one of the cancers in the above list?
6. Have there been diagnosed in your father's brothers or sisters, or your father's parents more than one of the cancers in the above list?
- 30

**Part C: Refer to the list of relatives below for responses only to questions in Part C**

- |    |                                    |   |
|----|------------------------------------|---|
|    | You                                | Your mother                                       |
| 35 | Your sisters or brothers & uncles) | Your mother's sisters or brothers (maternal aunts |
|    | Your children                      | Your mother's parents (maternal grandparents)     |
7. Have there been diagnosed in these relatives 2 or more identical types of cancer? Do not count "simple" skin cancer, also called basal cell or squamous cell skin cancer.
- 40 8. Is there a total of 4 or more of any cancers in the list of relatives above other than "simple" skin cancers?

**Part D: Refer to the list of relatives below for responses only to questions in Part D.**

- |    |                                      |   |
|----|--------------------------------------|---|
| 45 | You                                  | Your father                                       |
|    | Your sisters or brothers and uncles) | Your father's sisters or brothers (paternal aunts |
| 50 | Your children                        | Your father's parents (paternal grandparents)     |
9. Have there been diagnosed in these relatives 2 or more identical types of cancer? Do not count "simple" skin cancer, also called basal cell or squamous cell skin cancer.
- 55 10. Is there a total of 4 or more of any cancers in the list of relatives above other than "simple" skin cancers?

NOT FURNISHED UPON FILING

NO PRESENTADO/(A) EN EL MOMENTO DE LA PRESENTACIÓN

NON SOUMIS(E) AU MOMENT DU DÉPÔT

NOT FURNISHED UPON FILING

NO PRESENTADO/(A) EN EL MOMENTO DE LA PRESENTACIÓN

NON SOUMIS(E) AU MOMENT DU DÉPÔT

**TABLE II**  
**BRCA2 PRIMER SEQUENCES**

Exon	Label	SEQUENCE (5' TO 3') NOTE: M13 TAIL INCLUDED M13 FORWARD = TGT AAA ACG ACG GCC AGT M13 REVERSE = CAG GAA ACA GCT ATG ACC	Oligo Length	PCR Product Length	SEQ. ID. Number
2	BRCA2-2F	5'-TGA GTT TTA CCT CAG TCA CA-3'	20	263	14
2	BRCA2-2R/M 13R	5'-CAG GAA ACA GCT ATG ACC CTG TGA CGT ACT GGG TTT TTA GC-3'	41		15
3	BRCA2-3FII	5'-GAT CTT TAA CTG TTC TGG GTC ACA-3'	24	364	16
3	BRCA2-3RII	5'-CCC AGC ATG ACA CAA TTA ATG A-3'	22		17
4	BRCA2-4F/M 13F	5'-TGT AAA ACG ACG GCC AGT AGA ATG CAA ATT TAT AAT CCA GAG TA-3'	44	268	18
4	BRCA2-4R-1A	5'-ATC AGA TTC ATC TTT ATA GAA C-3'	22		19
5&6	BRCA2-5+6F/M13F	5'-TGT AAA ACG ACG GCC AGT TGT GTT GGC ATT TTA AAC ATC A-3'	40	453	20
5&6	BRCA2-5+6R/M13R	5'-CAG GAA ACA GCT ATG ACC CAG GGC AAA GGT ATA ACG CT-3'	38		21
7	BRCA2-7F/M13F	5'-TGT AAA ACG ACG GCC AGT TAA GTG AAA TAA AGA GTG AA-3'	38	248	22
7	BRCA2-7R/M13R	5'-CAG GAA ACA GCT ATG ACC AGA AGT ATT AGA GAT GAC-3'	36		23
8	BRCA2-8F/M13F	5'-TGT AAA ACG ACG GCC AGT GCC ATA TCT TAC CAC CTT GTG A-3'	40	319	24
	BRCA2-8FIA	5'-TTG CAT TCT AGT GAT AAT ATA C-3'	22	143	25
8	BRCA2-8RIA	5'-AAT TGT TAG CAA TTT CAA C-3'	19		26
9	BRCA2-9F/M13F	5'-TGT AAA ACG ACG GCC AGT TGG ACC TAG GTT GAT TGC AGA T-3'	40	338	27
9	BRCA2-9R/M13R	5'-CAG GAA ACA GCT ATG ACC TAA ACT GAG ATC ACG GGT GAC A-3'	40		28
10A	BRCA2-10AF	5'-GAA TAA TAT AAA TTA TAT GGC TTA-3'	24	255	29
10A	BRCA2-10AR/M13R	5'-CAG GAA ACA GCT ATG ACC CCT AGT CTT GCT AGT TCT T-3'	37		30
10B	BRCA2-10BF/M13F	5'- TGT AAA ACG ACG GCC AGT ARC TGA AGT GGA ACC AAA TGA TAC-3'	42	621	31

TABLE II  
BRCA2 PRIMER SEQUENCES

Exon	Label	SEQUENCE (5' TO 3') NOTE: M13 TAIL INCLUDED M13 FORWARD = TGT AAA ACG ACG GCC AGT M13 REVERSE = CAG GAA ACA GCT ATG ACC	Oligo Length	PCR Product Length	SEQ. ID. Number
10B	BRCA2-10BR/M13R	5'-CAG GAA ACA GCT ATG ACC ACG TGG CAA AGA ATT CTC TGA AGT AA-3'	44		32
10C	BRCA2-10CF/M13F	5'-TGT AAA ACG ACG GCC AGT CAG CAT CTT GAA TCT CAT ACA G-3'	40	508	33
10C	BRCA2-10CRII	5'-AGA CAG AGG TAC CTG AAT C-3'	19		34
11	BRCA2-11AF-M13	5'-TGT AAA ACG ACG GCC AGT TGG TAC TTT AAT TTT GTC ACT T-3'	40	304	35
11	BRCA2-11AR-M13	5'-CAG GAA ACA GCT ATG ACC TGC AGG CAT GAC AGA GAA T-3'	37		36
11	BRCA2-11BF	5'-AAG AAG CAA AAT GTA ATA AGG A-3'	22	411	37
11	BRCA2-11BR	5'-CAT TTA AAG CAC ATA CAT CTT G-3'	22		38
11	BRCA2-11CF	5'-TCT AGA GGC AAA GAA TCA TAC-3'	21	349	39
11	BRCA2-11CR	5'-CAA GAT TAT TCC TTT CAT TAG C-3'	22		40
11	BRCA2-11DF	5'-AAC CAA AAC ACA AAT CTA AGA G-3'	22	344	41
11	BRCA2-11DR	5'-GTC ATT TTT ATA TGC TGC TTT AC-3'	23		42
11	BRCA2-11EF	5'-GGT TTT ATA TGG AGA CAC AGG-3'	21	369	43
11	BRCA2-11ER	5'-GTA TTT ACA ATT TCA ACA CAA GC-3'	23		44
11	BRCA2-11FF	5'-ATC ACA GTT TTG GAG GTA GC-3'	20	368	45
11	BRCA2-11FR	5'-CTG ACT TCC TGA TTC TTC TAA-3'	21		46
11	BRCA2-11GF	5'-CTC AGA TGT TAT TTT CCA AGC-3'	21	366	47
11	BRCA2-11GR	5'-CTG TTA AAT AAC CAG AAG CAC-3'	21		48
11	BRCA2-11HF	5'-AGG TAG ACA GCA GCA AGC-3'	18	360	49
11	BRCA2-11HR	5'-GTA ATA TCA GTT GGC ATT TAT T-3'	22		50
11	BRCA2-11IF	5'-TGC AGA GGT ACA TCC AAT AAG-3'	21	326	51



TABLE II  
BRCA2 PRIMER SEQUENCES

Exon	Label	SEQUENCE (5' TO 3') NOTE: M13 TAIL INCLUDED M13 FORWARD = TGT AAA ACG ACG GCC AGT M13 REVERSE = CAG GAA ACA GCT ATG ACC	Oligo Length	PCR Product Length	SEQ. ID. Number
11	BRCA2-11IR	5'-GAT CAG TAA ATA GCA AGT CCG-3'	21		52
11	BRCA2-11JF	5'-TAC TGA AAA TGA AGA TAA CAA AT-3'	23	477	53
11	BRCA2-11JR	5'-ATT TTG TTC TTT CTT ATG TCA G-3'	22		54
11	BRCA2-11KF-M13	5'-TGT AAA ACG ACG GCC AGT CTA AAA CGG AGC AA-3'	35	382	55
11	BRCA2-11KR-M13	5'-CAG GAA ACA GCT ATG ACC GTA TGA AAA CCC AAC AG-3'	35		56
11	BRCA2-11LF	5'-CAC AAA ATA CTG AAA GAA AGT G-3'	22	374	57
11	BRCA2-11LR	5'-GGC ACC ACA GTC TCA ATA G-3'	19		58
11	BRCA2-11MF	5'-GCA AAG ACC CTA AAG TAC AG-3'	20	409	59
11	BRCA2-11MR	5'-CAT CAA ATA TTC CTT CTC TAA G-3'	22		60
11	BRCA2-11NF-M13	5'-TGT AAA ACG ACG GCC AGT GAA AAT TCA GCC TTA GC-3'	35	306	61
11	BRCA2-11NR-M13	5'-CAG GAA ACA GCT ATG ACC ATC AGA ATG GTA GGA AT-3'	35		62
11	BRCA2-11OF	5'-GTA CTA TAG CTG AAA ATG ACA A-3'	22	383	63
11	BRCA2-11OR	5'-ACC ACT GGC TAT CCT AAA TG-3'	20		64
11	BRCA2-11PF	5'-TGA AGA TAT TTG CGT TGA GG-3'	20	355	65
11	BRCA2-11PR	5'-GTC AGC AAA AAC CTT ATG TG-3'	20		66
11	BRCA2-11QF	5'-ACG AAA ATT ATG GCA GGT TGT-3'	21	337	67
11	BRCA2-11QR	5'-CTT GTC TTG CGT TTT GTA ATG-3'	21		68
11	BRCA2-11RF	5'-GCT TCA TAA GTC AGT CTC AT-3'	20	360	69
11	BRCA2-11RR	5'-TCA AAT TCC TCT AAC ACT CC-3'	20		70
11	BRCA2-11SF-M13	5'-TGT AAA ACG ACG GCC AGT TAC AGC AAG TGG AAA GC-3'	35	458	71

TABLE II  
BRCA2 PRIMER SEQUENCES

Exon	Label	SEQUENCE (5' TO 3') NOTE: M13 TAIL INCLUDED M13 FORWARD = TGT AAA ACG ACG GCC AGT M13 REVERSE = CAG GAA ACA GCT ATG ACC	Oligo Length	PCR Product Length	SEQ. ID. Number
11	BRCA2-11SR-M13	5'-CAG GAA ACA GCT ATG ACC AAG TTT CAG TTT TAC CAA T-3'	37		72
11	BRCA2-11TF	5'-GTT CTT CAG AAA ATA ATC ACT C-3'	22	344	73
11	BRCA2-11TR	5'-TGT AAA AAG AGA ATG TGT GGC-3'	21		74
11	BRCA2-11UF-M13	5'-TGT AAA ACG ACG GCC AGT ACT TTT TCT GAT GTT CCT GTG-3'	39	328	75
11	BRCA2-11UR-M13	5'-CAG GAA ACA GCT ATG ACC TAA AAA TAG TGA TTG GCA ACA-3'	39		76
12	BRCA2-12F/M13F	5'-TGT AAA ACG ACG GCC AGT AGT GGT GTT TTA AAG TGG TCA AAA-3'	42	391	77
12	BRCA2-12R/M13R	5'-CAG GAA ACA GCT ATG ACC GGA TCC ACC TGA GGT CAG AAT A-3'	40		78
13	BRCA2/13-2F	5'-TAA CAT TTA AGC ATC CGT TAC-3'	21	310	79
13	BRCA2/13-2R	5'-AAA CGA GAC TTT TCT CAT ACT GTA TTA G-3'	28		80
14	BRCA2-14F	5'-ACC ATG TAG CAA ATG AGG GTC T-3'	22	391	81
14	BRCA2-14AR	5'-GCT TTT GTC TGT TTT CCT CCA A-3'	22		82
15	BRCA2-15-2F	5'-CCA GGG GTT GTG CTT TTT AAA-3'	21	284	83
15	BRCA2-15FUT/M13-R	5'-CAG GAA ACA GCT ATG ACC ACT CTG TCA TAA AAG CCA TC-3'	38		84
16	BRCA2-16AF	5'-TTT GGT TTG TTA TAA TTG TTT TTA-3'	24	394	85
16	BRCA2-16AR	5'-CCA ACT TTT TAG TTC GAG AG-3'	20		86
17	BRCA2-17F	5'-TTC AGT ATC ATC CTA TGT G-3'	19	282	87
17	BRCA2-17AR	5'-AGA AAC CTT AAC CCA TAC TG-3'	20		88
18	BRCA2-18FUT/M13-AF	5'-TGT AAA ACG ACG GCC AGT GAA TTC TAG AGT CAC ACT TCC-3'	39	275	89
18	BRCA2-18R/M13R	5'-CAG GAA ACA GCT ATG ACC TTT AAC TGA ATC AAT GAC TG-3'	38		90
19	BRCA2-19F/M13F	5'-TGT AAA ACG ACG GCC AGT AAG TGA ATA TTT TTA AGG CAG TT-3'	41	355	91

TABLE II  
BRCA2 PRIMER SEQUENCES

Exon	Label	SEQUENCE (5' TO 3') NOTE: M13 TAIL INCLUDED M13 FORWARD = TGT AAA ACG ACG GCC AGT M13 REVERSE = CAG GAA ACA GCT ATG ACC	Oligo Length	PCR Product Length	SEQ. ID. Number
19	BRCA2-19FUT/M13-R	5'-CAG GAA ACA GCT ATG ACC AAG AGA CCG AAA CTC CAT CTC-3'	39		92
20	BRCA2-20F/M13F	5'-TGT AAA ACG ACG GCC AGT CAC TGT GCC TGG CCT GAT AC-3'	38	296	93
20	BRCA2-20R/M13R	5'-CAG GAA ACA GCT ATG ACC ATG TTA AAT TCA AAG TCT CTA-3'	39		94
21	BRCA2-21F/M13F	5'-TGT AAA ACG ACG GCC AGT GGG TGT TTT ATG CTT GGT TCT-3'	39	304	95
21	BRCA2-21R/M13R	5'-CAG GAA ACA GCT ATG ACC CAT TTC AAC ATA TTC CTT CCT G-3'	40		96
22	BRCA2-22F-1A	5'-AAC CAC ACC CTT AAG ATG A-3'	19	453	97
22	BRCA2-22R-1A	5'-GCA TTA GTA GTG GAT TTT GC-3'	20		98
23	BRCA2-23FII	5'-TCA CTT CCA TTG CAT C-3'	16	290	99
23	BRCA2-23RII	5'-TGC CAA CTG GTA GCT CC-3'	17		100
24	BRCA2-24 2F	5'-TAC AGT TAG CAG CGA CAA AA-3'	20	373	101
24	BRCA2-24R/M13R	5'-CAG GAA ACA GCT ATG ACC ATT TGC CAA CTG GTA GCT CC-3'	38		102
25	BRCA2-25F-7/23	5'-GCT TTC GCC AAA TTC AGC TA-3'	20	427	103
25	BRCA2-25R-7/23	5'-TAC CAA AAT GTG TGG TGA TG-3'	20		104
26	BRCA2/26-2F	5'-AAT CAC TGA TAC TGG TTT TG-3'	20	530	105
26	BRCA2/26-2R	5'-TAT ACT TAC AGG AGC CAC AT-3'	20		106
27A	BRCA2-27AF-1A	5'-CTG TGT GTA ATA TTT GCG-3'	18	495	107
27A	BRCA2-27AR/M13R	5'-CAG GAA ACA GCT ATG ACG GCA AGT TCT TCG TCA GCT ATT G-3'	40		108
27B	BRCA2-27BF/M13F	5'-TGT AAA AC-3 ACG GCC AGT GAA TTC TCC TCA GAT GAC TCC A-3'	40	417	109
27B	BRCA2-27BR/M13R	5'-CAG GAA ACA GCT ATG ACC TCT TTG CTC ATT GTG CAA CA-3'	38		110

TABLE III  
NORMAL PANEL TYPING

Position nt/codon	Nucleotide Change	Amino Acid Change	1	2	3	4	5	Frequency
1093/289	<u>A</u> AT → <u>C</u> AT	Asn → His	A/A	A/C	A/A	A/A	A/C	A = .8 C = .2
1342/372	<u>A</u> AT → <u>C</u> AT	Asn → His	A/C	A/A	A/C	A/C	A/C	A = 0.6 C = 0.4
1593/455	T <u>C</u> A → T <u>C</u> <u>G</u>	Ser → Ser	A/A	A/A	A/A	A/A	A/G	A = 0.9 G = 0.1
2457/743	<u>C</u> AT → <u>C</u> A <u>C</u>	His → His	T/T	C/T	T/T	T/T	C/T	T = 0.8 C = 0.2
2908/894	<u>G</u> TA → <u>A</u> TA	Val → Ile	G/G	G/G	G/G	G/G	A/G	G = 0.9 A = 0.1
3199/991	<u>A</u> AC → <u>G</u> AC	Asn → Asp	A/A	A/G	A/A	A/A	A/G	A = 0.8 G = 0.2

TABLE III  
NORMAL PANEL TYPING

Position nt/codon	Nucleotide Change	Amino Acid Change	1	2	3	4	5	Frequency
3624/1132	<u>AAA</u> → <u>AAG</u>	Lys → Lys	A/A	A/G	A/A	A/G	A/A	A = 0.8 G = 0.2
4035/1269	<u>GTT</u> → <u>GTC</u>	Val → Val	C/T	T/T	T/T	T/T	T/T	T = 0.9 C = 0.1
7470/2414	<u>TCA</u> → <u>TCG</u>	Ser → Ser	A/A	A/G	A/A	A/G	A/A	A = 0.8 G = 0.2
9079/2951	<u>GCC</u> → <u>ACC</u>	Ala → Thr	G/G	G/G	G/G	G/G	A/G	G = 0.9 A = 0.1

**EXAMPLE 2****Determination Of A Normal Individual Using BRCA2<sup>(OMI 1-5)</sup> and The Ten Polymorphisms For Reference**

5 A person skilled in the art of genetic susceptibility testing will find the present invention useful for:

- a) identifying individuals having a normal BRCA2 gene;
- b) avoiding misinterpretation of normal polymorphisms found in the normal population.

10 Sequencing was carried out as in EXAMPLE 1 using a blood sample from the patient in question. However, the BRCA2<sup>(omi1-5)</sup> sequences were used for reference and any polymorphic sites seen in the patient were compared to the nucleic acid sequences listed above for normal codons at each polymorphic site. A normal sample is one which is comparable to the BRCA2<sup>(omi1-5)</sup> sequences and contains only  
 15 minor variations which occur at minor polymorphic sites. The allelic variations which occur at each of the polymorphic sites are paired here for reference.

- AAT (Asn) and CAT (His) at position 1093 (codon 289)
- CAT (His) and AAT (Asn) at position 1342 (codon 372)
- 20 • TCA (Ser) and TCG (Ser) at position 1593 (codon 455)
- CAT (His) and CAC (His) at position 2457 (codon 743)
- GTA (Val) and ATA (Ile) at position 2908 (codon 894)
- AAC (Asn) and GAC (Asp) at position 3199 (codon 991)
- AAA (Lys) and AAG (Lys) at position 3624 (codon 1132)
- 25 • GTT (Val) and GTC (Val) at position 4035 (codon 1269)
- TCA (Ser) and TCG (Ser) at position 7470 (codon 2414)
- GCC (Ala) and ACC (Thr) at position 9079 (codon 2951)

30 The availability of these polymorphic pairs provides added assurance that one skilled in the art can correctly interpret the polymorphic variations without mistaking a normal variation for a mutation.

All exons of the BRCA2 gene are subjected to direct dideoxy sequence analysis by asymmetric amplification using the polymerase chain reaction (PCR) to generate a single stranded product amplified from this DNA sample. Shuldiner, et

*al.*, *Handbook of Techniques in Endocrine Research*, p. 457-486, DePablo, F., Scanes, C., eds., Academic Press, Inc., 1993. Fluorescent dye is attached for automated sequencing using the Taq Dye Terminator Kit (Perkin-Elmer® cat# 401628). DNA sequencing is performed in both forward and reverse directions on an Applied Biosystems, Inc. (ABI) automated sequencer (Model 377). The software used for analysis of the resulting data is "Sequence Navigator" purchased through ABI.

1. Polymerase Chain Reaction (PCR) Amplification

The PCR primers used to amplify a patient's sample BRCA2 gene are listed in TABLE II. The primers were synthesized on a DNA/RNA Synthesizer Model 394®. Thirty-five cycles of amplification are performed, each consisting of denaturing (95°C; 30 seconds), annealing (55°C; 1 minute), and extension (72°C; 90 seconds), except during the first cycle in which the denaturing time is increased to 5 minutes and during the last cycle in which the extension time is increased to 5 minutes.

PCR products are purified using Qia-quick® PCR purification kits (Qiagen®, cat# 28104; Chatsworth, CA). Yield and purity of the PCR product are determined spectrophotometrically at OD<sub>260</sub> on a Beckman DU 650 spectrophotometer.

2. Dideoxy Sequence Analysis

Fluorescent dye is attached to PCR products for automated sequencing using the Taq Dye Terminator Kit (Perkin-Elmer® cat# 401628). DNA sequencing is performed in both forward and reverse directions on an Applied Biosystems, Inc. (ABI) Foster City, CA., automated sequencer (Model 377). The software used for analysis of the resulting data is "Sequence Navigator®" purchased through ABI. The BRCA2<sup>(omi 1-5)</sup> sequences were entered sequentially into the Sequence Navigator software as the standards for comparison. The Sequence Navigator software compares the patient sample sequence to each BRCA2<sup>(omi 1-5)</sup> standard, base by base. The Sequence Navigator highlights all differences between the standards (omi 1-5) and the patient's sample sequence.

A first technologist checks the computerized results by comparing visually the BRCA2<sup>(omi 1-5)</sup> standards against the patient's sample, and again highlights any differences between the standard and the sample. The first primary technologist  
5 then interprets the sequence variations at each position along the sequence. Chromatograms from each sequence variation are generated by the Sequence Navigator and printed on a color printer. The peaks are interpreted by the first primary technologist and a second primary technologist. A secondary technologist then reviews the chromatograms. The results are finally interpreted by a geneticist.  
10 In each instance, a variation is compared to known normal polymorphisms for position and base change.

### 3. Results

The patient's BRCA2 sequence was found to be heterozygous at seven  
15 nucleotide positions: 1093 (A/C), 1342 (A/C), 1593 (A/G), 2457 (C/T), 2908 (A/G), 3199 (A/G) and 9079 (A/G). In addition, this changes five amino acids in the polypeptide product: Asn to His at codon 289, Asn to His at codon 372, Val to Ile at codon 894, Asn to Asp at codon 991, and Ala to Thr at codon 2951. The question arises whether any or all of these changes have significance to the patient.  
20 Comparison of the patient's results to the BRCA<sup>(omi 1-5)</sup> haplotypes demonstrates that it matches one of the BRCA2 omi standards (#5), and thus the patient sample is interpreted as carrying a normal gene sequence without causing any elevation in their risk status for breast cancer.

### 25 EXAMPLE 3

#### **DETERMINING THE PRESENCE OF A MUTATION IN EXON 11 OF THE BRCA2 GENE USING BRCA2(omi1-5)**

A person skilled in the art of genetic susceptibility testing will find the present invention useful for determining the presence of a known or previously unknown  
30 mutation in the BRCA2 gene. A list of mutations of BRCA2 is publicly available in the Breast Cancer Information Core at [http://www.nchgr.nih.gov/dir/lab\\_transfer/bic](http://www.nchgr.nih.gov/dir/lab_transfer/bic). This data site became publicly available on November 1, 1995. Friend, S. et al. *Nature Genetics* 11:238, (1995).



In this example, a mutation in exon 11 is characterized by amplifying the region of the mutation with a primer set which amplifies the region of the mutation. Sequencing was carried out as in Example 1 using a blood sample from the patient in question. Specifically, exon 11 of the BRCA2 gene is subjected to direct dideoxy sequence analysis by asymmetric amplification using the polymerase chain reaction (PCR) to generate a single stranded product amplified from this DNA sample. Shuldiner, *et al.*, *Handbook of Techniques in Endocrine Research*, p. 457-486, DePablo, F., Scanes, C., eds., Academic Press, Inc., 1993. Fluorescent dye is attached for automated sequencing using the Taq Dye Terminator Kit (Perkin-Elmer® cat# 401628). DNA sequencing is performed in both forward and reverse directions on an Applied Biosystems, Inc. (ABI) automated sequencer (Model 377). The software used for analysis of the resulting data is "Sequence Navigator" purchased through ABI.

15

#### 1. Polymerase Chain Reaction (PCR) Amplification

Genomic DNA (100 nanograms) extracted from white blood cells of the subject is amplified in a final volume of 25 microliters containing 1 microliter (100 nanograms) genomic DNA, 2.5 microliters 10X PCR buffer (100 mM Tris, pH 8.3, 500 mM KCl, 1.2 mM MgCl<sub>2</sub>), 2.5 microliters 10X dNTP mix (2 mM each nucleotide), 2.5 microliters forward primer (BRCA2-11Q-F, 10 micromolar solution), 2.5 microliters reverse primer (BRCA2-11Q-R, 10 micromolar solution), and 1 microliter Taq polymerase (5 units), and 13 microliters of water.

The PCR primers used to amplify segment Q of exon 11 (where the mutation 6174delT is found) are as follows:

BRCA2-11Q-F: 5'- ACG' AAA' ATT' ATG' GCA' GGT' TGT-3'

BRCA2-11Q-R: 5'- CTT' GTC' TTG' CGT' TTT' GTA' ATG-3'

30

The primers are synthesized on an DNA/RNA Synthesizer Model 394®. Thirty-five cycles are performed, each consisting of denaturing (95°C; 30 seconds), annealing (55°C; 1 minute), and extension (72°C; 90 seconds), except during the

first cycle in which the denaturing time is increased to 5 minutes, and during the last cycle in which the extension time is increased to 5 minutes.

5 PCR products are purified using Qia-quick<sup>®</sup> PCR purification kits (Qiagen<sup>®</sup>, cat# 28104; Chatsworth, CA). Yield and purity of the PCR product are determined spectrophotometrically at OD<sub>260</sub> on a Beckman DU 650 spectrophotometer.

## 2. Dideoxy Sequence Analysis

Fluorescent dye is attached to PCR products for automated sequencing using  
10 the Taq Dye Terminator Kit (Perkin-Elmer<sup>®</sup> cat# 401628). DNA sequencing is performed in both forward and reverse directions on an Applied Biosystems, Inc. (ABI) Foster City, CA., automated sequencer (Model 377). The software used for analysis of the resulting data is "Sequence Navigator<sup>®</sup>" purchased through ABI. The BRCA2<sup>(omi 1-5)</sup> sequence is entered into the Sequence Navigator software as the  
15 Standard for comparison. The Sequence Navigator software compares the sample sequence to the BRCA2<sup>(omi)</sup> standard, base by base. The Sequence Navigator highlights all differences between the BRCA2<sup>(omi)</sup> normal DNA sequence and the patient's sample sequence.

A first technologist checks the computerized results by comparing visually the  
20 BRCA2<sup>(omi 1-5)</sup> standard against the patient's sample, and again highlights any differences between the standard and the sample. The first primary technologist then interprets the sequence variations at each position along the sequence. Chromatograms from each sequence variation are generated by the Sequence Navigator and printed on a color printer. The peaks are interpreted by the first  
25 primary technologist and a second primary technologist. A secondary technologist then reviews the chromatograms. The results are finally interpreted by a geneticist. In each instance, a sequence variation is compared to known normal polymorphisms for position and base change. The ten frequent polymorphisms which occur in BRCA2 are:

30

- AAT (Asn) and CAT (His) at position 1093 (codon 289)
- CAT (His) and AAT (Asn) at position 1342 (codon 372)
- TCA (Ser) and TCG (Ser) at position 1593 (codon 455)

- CAI (His) and CAC (His) at position 2457 (codon 743)
- GTA (Val) and ATA (Ile) at position 2908 (codon 894)
- AAC (Asn) and GAC (Asp) at position 3199 (codon 991)
- 5 • AAA (Lys) and AAG (Lys) at position 3624 (codon 1132)
- GTI (Val) and GTC (Val) at position 4035 (codon 1269)
- TCA (Ser) and TCG (Ser) at position 7470 (codon 2414)
- GCC (Ala) and ACC (Thr) at position 9079 (codon 2951)

### 10 3. Results

Using the above PCR amplification and standard fluorescent sequencing technology, the 6174delT mutation may be found. Mutations are noted by the length of non-matching sequence variation. Such a lengthy mismatch pattern occurs with deletions and insertions. This mutation is named in accordance with the suggested  
15 nomenclature for naming mutations, Beaudet, A *et al.*, *Human Mutation* 2:245-248, (1993). The 6174delT mutation at codon 1982 of the BRCA2 gene lies in segment "Q" of exon 11. The DNA sequence results demonstrate the presence of a one base pair deletion of a T at nucleotide 6174 of the BRCA2<sup>(om1 1-5)</sup> sequences. This mutation interrupts the normal reading frame of the BRCA2 transcript, resulting in  
20 the appearance of an in-frame terminator (TAG) at codon position 2003. This mutation is, therefore, predicted to result in a truncated, and most likely, non-functional protein.

### EXAMPLE 4

#### 25 GENERATION OF MONOCLONAL AND POLYCLONAL ANTIBODIES USING GST-BRCA2 FUSION PROTEIN AS AN IMMUNOGEN

DNA primers are used to amplify a fragment of BRCA2 using PCR technology. The product is then digested with suitable restriction enzymes and fused in frame with the gene encoding glutathione S-transferase (GST) in  
30 *Escherichia coli* using GST expression vector pGEX (Pharmacia Biotech Inc.) The expression of the fusion protein is induced by the addition of isopropyl- $\beta$ -thiogalactopyranoside. The bacteria are then lysed and the overexpressed fusion protein is purified with glutathione-sepharose beads. The fusion protein is then verified by SDS/PAGE gel and N-terminus protein sequencing. The purified protein

is used to immunize rabbits according to standard procedures described in Harlow & Lane (1988). Polyclonal antibody is collected from the serum several weeks after and purified using known methods in the art. Monoclonal antibodies against all or  
5 fragments of BRCA2 protein, polypeptides, or functional equivalents are obtained using hybridoma technology, see also Harlow & Lane (1988). The BRCA2 protein or polypeptide is coupled to the carrier keyhole limpet hemocyanin in the presence of glutaraldehyde. The conjugated immunogen is mixed with an adjuvant and injected into rabbits. Spleens from antibody-containing rabbits are removed. The B-cells  
10 isolated from spleen are fused to myeloma cells using polyethylene glycol (PEG) to promote fusion. The hybrids between the myeloma and B-cells are selected and screened for the production of antibodies to immunogen BRCA2 protein or polypeptide. Positive cells are recloned to generate monoclonal antibodies.

#### 15 **EXAMPLE 5**

##### **DETECTION OF BRCA2 EXPRESSION IN HUMAN TISSUES AND CELL LINES**

The expression of BRCA2 in human tissues is determined using Northern blot analysis. Human tissues include those from pancreas, testis, prostate, ovary, breast, small intestine, and colon are obtained from Clontech Laboratories, Inc., Palo  
20 Alto, CA. The poly(A)+ mRNA Northern blots from different human tissues is hybridized to BRCA2 cDNA probes according to manufacture protocol. The expression level is further conformed by RT-PCR using oligo-d(T) as a primer and other suitable primers.

For Northern Blot analysis of cancer cell lines, the human ovarian cancer cell  
25 line SKOV-3 and the human breast cancer cell line MCF-7 are obtained from the American Type Culture Collection. Total RNA is prepared by lysing cell in the presence of guanidinium isocyanate. Poly(A)+ mRNA is isolated using the PolyAtract mRNA isolation system from Promega, Madison, WI. The isolated RNA is then electrophoresed under denaturing conditions and transferred to Nylon  
30 membrane. The probe used for Northern blot is a fragment of BRCA2 sequence obtained by PCR amplification. The probes are labeled with [ $\alpha$ -<sup>32</sup>P] dCTP using a random-primed labeling kit (Amersham Life Science, Arlington Heights, IL).

**EXAMPLE 6****EXPRESSION OF THE BRCA2 PROTEIN**

The whole-cell extracts of BRCA2 transfected cells are subjected to immunoprecipitation and immunoblotting to determine the BRCA2 protein level. The BRCA2 protein or polypeptide is immunoprecipitated using anti-BRCA2 antibodies prepared according to Example 4. Samples are then fractionated using SDS/PAGE gel and transferred to nitrocellulose. Western blot of the BRCA2 protein or polypeptide is performed with the indicated antibodies. Antibody reaction is revealed using enhanced chemiluminescence reagents (Dupont New England Nuclear, Boston, MA).

**EXAMPLE 7****USE OF THE BRCA2<sup>(omi1-5)</sup> GENE THERAPY**

The growth of ovarian or breast cancer may be arrested by increasing the expression of the BRCA2 gene where inadequate expression of that gene is responsible for hereditary ovarian or breast cancer. Gene therapy may be performed on a patient to reduce the size of a tumor. The LXS vector may be transformed with a BRCA2<sup>(omi1-5)</sup> coding sequence as presented SEQ ID NO:4, 6, 8, 10, or 12 or a fragment thereof.

**Vector**

The LXS vector is transformed with a fragment of the wildtype BRCA2<sup>(omi1-5)</sup> coding sequence as set forth in SEQ ID NO:4, 6, 8, 10, or 12. The LXS-BRCA2<sup>(omi1-5)</sup> retroviral expression vector is constructed by cloning a *SaI* I linker BRCA2<sup>(omi1-5)</sup> cDNA or fragments thereof into the *Xho* I site of the vector LXS. Constructs are confirmed by DNA sequencing. See Holt et al., *Nature Genetics* 12: 298-302 (1996). Retroviral vectors are manufactured from viral producer cells using serum free and phenol-red free conditions and tested for sterility, absence of specific pathogens, and absence of replication-competent retrovirus by standard assays. Retrovirus is stored frozen in aliquots which have been tested.

Patients receive a complete physical exam, blood, and urine tests to determine overall health. They may also have a chest X-ray, electrocardiogram, and appropriate radiologic procedures to assess tumor stage.

Patients with metastatic ovarian cancer are treated with retroviral gene therapy by infusion of recombinant LXSN-BRCA2<sup>(omi1-5)</sup> retroviral vectors into peritoneal sites containing tumor, between 10<sup>9</sup> and 10<sup>10</sup> viral particles per dose.

5 Blood samples are drawn each day and tested for the presence of retroviral vector by sensitive polymerase chain reaction (PCR)-based assays. The fluid which is removed is analyzed to determine:

1. The percentage of cancer cells which are taking up the recombinant LXSN-BRCA2<sup>(omi1-5)</sup> retroviral vector combination. Successful transfer of BRCA1  
10 gene into cancer cells has been shown by both RT-PCR analysis and *in situ* hybridization. RT-PCR is performed with by the method of Thompson et al., *Nature Genetics* 9: 444-450 (1995), using primers derived from a BRCA2<sup>(omi1-5)</sup> coding sequence as in SEQ ID NO:4, 6, 8, 10, or 12 or fragments thereof. Cell lysates are prepared and immunoblotting is performed by the method of Jensen et al., *Nature*  
15 *Genetics* 12: 303-308 (1996) and Jensen et al., *Biochemistry* 31: 10887-10892 (1992).

2. Presence of programmed cell death using APOTAG<sup>®</sup> *in situ* apoptosis detection kit (ONCOR, INC., Gaithersburg, Maryland) and DNA analysis.

3. Measurement of BRCA2 gene expression by slide immunofluorescence or  
20 Western blot.

Patients with measurable disease are also evaluated for a clinical response to LXSN-BRCA2<sup>(omi1-5)</sup> especially those that do not undergo a palliative intervention immediately after retroviral vector therapy. Fluid cytology, abdominal girth, CT scans of the abdomen, and local symptoms are followed.

25

For other sites of disease, conventional response criteria are used as follows:

1. Complete Response (CR), complete disappearance of all measurable lesions and of all signs and symptoms of disease for at least 4 weeks.
2. Partial Response (PR), decrease of at least 50% of the sum of the products of  
30 the 2 largest perpendicular diameters of all measurable lesions as determined by 2 observations not less than 4 weeks apart. To be considered a PR, no new lesions should have appeared during this period and none should have increased in size.
3. Stable Disease, less than 25% change in tumor volume from previous evaluations.

4. Progressive Disease, greater than 25% increase in tumor measurements from prior evaluations. The number of doses depends upon the response to treatment.

5 **EXAMPLE 8**

**PROTEIN REPLACEMENT THERAPY**

Therapeutically elevated level of functional BRCA2 protein may alleviate the absence or reduced endogenous BRCA2 tumor suppressing activity. Breast or ovarian cancer is treated by the administration of a therapeutically effective amount  
10 of the BRCA2 protein, a polypeptide, or its functional equivalent in a pharmaceutically acceptable carrier. Clinically effective delivery method is applied either locally at the site of the tumor or systemically to reach other metastasized locations with known protocols in the art. These protocols may employ the methods of direct injection into a tumor or diffusion using time release capsule. A  
15 therapeutically effective dosage is determined by one of skill in the art.

Breast or ovarian cancer may be prevented by the administration of a prophylactically effective amount of the BRCA2 protein, polypeptide, or its functional equivalent in a pharmaceutically acceptable carrier. Individuals with known risk for breast or ovarian cancer are subjected to protein replacement therapy to prevent  
20 tumorigenesis or to decrease the risk of cancer. Elevated risk for breast and ovarian cancer includes factors such as carriers of one or more known BRCA1 and BRCA2 mutations, late child bearing, early onset of menstrual period, late occurrence of menopause, and certain high risk dietary habits. Clinically effective delivery method is used with known protocols in the art, such as administration into peritoneal cavity,  
25 or using an implantable time release capsule. A prophylactically effective dosage is determined by one of skill in the art.

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Although the invention has been described with reference to the presently preferred embodiments, it should be understood that various modifications can be made without departing from the spirit of the invention. Accordingly, the invention is  
5 limited only by the following claims.

## SEQUENCE LISTING

5

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(ii) TITLE OF THE INVENTION: NOVEL CODING SEQUENCE HAPLOTYPES  
OF THE HUMAN BRCA2 GENE

20

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(v) COMPUTER READABLE FORM:

(A) MEDIUM TYPE: Diskette  
(B) COMPUTER: IBM Compatible  
(C) OPERATING SYSTEM: DOS  
35 (D) SOFTWARE: FastSEQ for Windows Version 2.0

(vi) CURRENT APPLICATION DATA:

(A) APPLICATION NUMBER:  
(B) FILING DATE:  
40 (C) CLASSIFICATION:

(vii) PRIOR APPLICATION DATA:

(A) APPLICATION NUMBER:  
45 (B) FILING DATE:

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60

## (2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 50 base pairs

(B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

5

(ii) MOLECULE TYPE: Genomic DNA  
 (ix) FEATURE:

(A) NAME/KEY: exon  
 (B) LOCATION: 1...50  
 (D) OTHER INFORMATION: Exon 5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

15 TCCTGTTGTT CTACAATGTA CACATGTAAC ACCACAAAGA GATAAGTCAG

50

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 182 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: Genomic DNA  
 (ix) FEATURE:

(A) NAME/KEY: exon  
 (B) LOCATION: 1...182  
 (D) OTHER INFORMATION: Exon 15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

35 ATTTAATTAC AAGTCTTCAG AATGCCAGAG ATATACAGGA TATGCGAATT AAGAAGAAAC 60  
 AAAGGCAACG CGTCTTTCCA CAGCCAGGCA GTCTGTATCT TGCAAAAACA TCCACTCTGC 120  
 CTCCAATCTC TCTGAAAGCA GCAGTAGGAG GCCAAGTTCC CTCTGCGTGT TCTCATAAAC 180  
 AG 182

(2) INFORMATION FOR SEQ ID NO:3:

40

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 188 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

45

(ii) MOLECULE TYPE: Genomic DNA  
 (ix) FEATURE:

50 (A) NAME/KEY: exon  
 (B) LOCATION: 1...188  
 (D) OTHER INFORMATION: Exon 16

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

55 CTGTATACGT ATGGCGTTTC TAAACATTGC ATAAAAATTA ACAGCAAAAA TGCAGAGTCT 60  
 TTTCAGTTTC ACACTGAAGA TTATTTTGGT AAGGAAAGTT TATGGACTGG AAAAGGAATA 120  
 CAGTTGGCTG ATGGTGGATG GCTCATACCC TCCAATGATG GAAAGGCTGG AAAAGAAGAA 180  
 TTTTATAG 188

60

(2) INFORMATION FOR SEQ ID NO:4:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 10485 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: cDNA

## (ix) FEATURE:

- (A) NAME/KEY: Coding Sequence  
 (B) LOCATION: 229...10482  
 (D) OTHER INFORMATION: BRCA2 (OMI1)

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

```

5      GGTGGCGCGA GCTTCTGAAA CTAGGCGGCA GAGGCGGAGC CGCTGTGGCA CTGCTGCGCC      60
      TCTGCTGCGC CTCGGGTGTC TTTTGCGGCG GTGGGTCGCC GCCGGGAGAA GCGTGAGGGG      120
      ACAGATTGTG GACCGGCGCG GTTTTGTCA GCTTACTCCG GCCAAAAAAG AACTGCACCT      180
20     CTGGAGCGGA CTTATTTACC AAGCATTGGA GGAATATCGT AGGTAAAA ATG CCT ATT      237
                                   Met Pro Ile
                                   1

      GGA TCC AAA GAG AGG CCA ACA TTT TTT GAA ATT TTT AAG ACA CGC TGC      285
25     Gly Ser Lys Glu Arg Pro Thr Phe Phe Glu Ile Phe Lys Thr Arg Cys
      5                                10                                15

      AAC AAA GCA GAT TTA GGA CCA ATA AGT CTT AAT TGG TTT GAA GAA CTT      333
30     Asn Lys Ala Asp Leu Gly Pro Ile Ser Leu Asn Trp Phe Glu Glu Leu
      20                                25                                30                                35

      TCT TCA GAA GCT CCA CCC TAT AAT TCT GAA CCT GCA GAA GAA TCT GAA      381
      Ser Ser Glu Ala Pro Pro Tyr Asn Ser Glu Pro Ala Glu Glu Ser Glu
      40                                45                                50

35     CAT AAA AAC AAC AAT TAC GAA CCA AAC CTA TTT AAA ACT CCA CAA AGG      429
      His Lys Asn Asn Asn Tyr Glu Pro Asn Leu Phe Lys Thr Pro Gln Arg
      55                                60                                65

40     AAA CCA TCT TAT AAT CAG CTG GCT TCA ACT CCA ATA ATA TTC AAA GAG      477
      Lys Pro Ser Tyr Asn Gln Leu Ala Ser Thr Pro Ile Ile Phe Lys Glu
      70                                75                                80

      CAA GGG CTG ACT CTG CCG CTG TAC CAA TCT CCT GTA AAA GAA TTA GAT      525
45     Gln Gly Leu Thr Leu Pro Leu Tyr Gln Ser Pro Val Lys Glu Leu Asp
      85                                90                                95

      AAA TTC AAA TTA GAC TTA GGA AGG AAT GTT CCC AAT AGT AGA CAT AAA      573
50     Lys Phe Lys Leu Asp Leu Gly Arg Asn Val Pro Asn Ser Arg His Lys
      100                               105                               110                               115

      AGT CTT CGC ACA GTG AAA ACT AAA ATG GAT CAA GCA GAT GAT GTT TCC      621
      Ser Leu Arg Thr Val Lys Thr Lys Met Asp Gln Ala Asp Asp Val Ser
      120                               125                               130

55     TGT CCA CTT CTA AAT TCT TGT CTT AGT GAA AGT CCT GTT GTT CTA CAA      669
      Cys Pro Leu Leu Asn Ser Cys Leu Ser Glu Ser Pro Val Val Leu Gln
      135                               140                               145

60     TGT ACA CAT GTA ACA CCA CAA AGA GAT AAG TCA GTG GTA TGT GGG AGT      717
      Cys Thr His Val Thr Pro Gln Arg Asp Lys Ser Val Val Cys Gly Ser
      150                               155                               160

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5	TTG TTT CAT ACA CCA AAG TTT GTG AAG GGT CGT CAG ACA CCA AAA CAT Leu Phe His Thr Pro Lys Phe Val Lys Gly Arg Gln Thr Pro Lys His 165 170 175	765
10	ATT TCT GAA AGT CTA GGA GCT GAG GTG GAT CCT GAT ATG TCT TGG TCA Ile Ser Glu Ser Leu Gly Ala Glu Val Asp Pro Asp Met Ser Trp Ser 180 185 190 195	813
15	AGT TCT TTA GCT ACA CCA CCC ACC CTT AGT TCT ACT GTG CTC ATA GTC Ser Ser Leu Ala Thr Pro Pro Thr Leu Ser Ser Thr Val Leu Ile Val 200 205 210	861
20	AGA AAT GAA GAA GCA TCT GAA ACT GTA TTT CCT CAT GAT ACT ACT GCT Arg Asn Glu Glu Ala Ser Glu Thr Val Phe Pro His Asp Thr Thr Ala 215 220 225	909
25	AAT GTG AAA AGC TAT TTT TCC AAT CAT GAT GAA AGT CTG AAG AAA AAT Asn Val Lys Ser Tyr Phe Ser Asn His Asp Glu Ser Leu Lys Lys Asn 230 235 240	957
30	GAT AGA TTT ATC GCT TCT GTG ACA GAC AGT GAA AAC ACA AAT CAA AGA Asp Arg Phe Ile Ala Ser Val Thr Asp Ser Glu Asn Thr Asn Gln Arg 245 250 255	1005
35	GAA GCT GCA AGT CAT GGA TTT GGA AAA ACA TCA GGG AAT TCA TTT AAA Glu Ala Ala Ser His Gly Phe Gly Lys Thr Ser Gly Asn Ser Phe Lys 260 265 270 275	1053
40	GTA AAT AGC TGC AAA GAC CAC ATT GGA AAG TCA ATG CCA AAT GTC CTA Val Asn Ser Cys Lys Asp His Ile Gly Lys Ser Met Pro Asn Val Leu 280 285 290	1101
45	GAA GAT GAA GTA TAT GAA ACA GTT GTA GAT ACC TCT GAA GAA GAT AGT Glu Asp Glu Val Tyr Glu Thr Val Val Asp Thr Ser Glu Glu Asp Ser 295 300 305	1149
50	TTT TCA TTA TGT TTT TCT AAA TGT AGA ACA AAA AAT CTA CAA AAA GTA Phe Ser Leu Cys Phe Ser Lys Cys Arg Thr Lys Asn Leu Gln Lys Val 310 315 320	1197
55	AGA ACT AGC AAG ACT AGG AAA AAA ATT TTC CAT GAA GCA AAC GCT GAT Arg Thr Ser Lys Thr Arg Lys Lys Ile Phe His Glu Ala Asn Ala Asp 325 330 335	1245
60	GAA TGT GAA AAA TCT AAA AAC CAA GTG AAA GAA AAA TAC TCA TTT GTA Glu Cys Glu Lys Ser Lys Asn Gln Val Lys Glu Lys Tyr Ser Phe Val 340 345 350 355	1293
65	TCT GAA GTG GAA CCA AAT GAT ACT GAT CCA TTA GAT TCA AAT GTA GCA Ser Glu Val Glu Pro Asn Asp Thr Asp Pro Leu Asp Ser Asn Val Ala 360 365 370	1341
70	CAT CAG AAG CCC TTT GAG AGT GGA AGT GAC AAA ATC TCC AAG GAA GTT His Gln Lys Pro Phe Glu Ser Gly Ser Asp Lys Ile Ser Lys Glu Val 375 380 385	1389
75	GTA CCG TCT TTG GCC TGT GAA TGG TCT CAA CTA ACC CTT TCA GGT CTA Val Pro Ser Leu Ala Cys Glu Trp Ser Gln Leu Thr Leu Ser Gly Leu 390 395 400	1437

	AAT GGA GCC CAG ATG GAG AAA ATA CCC CTA TTG CAT ATT TCT TCA TGT	1485
	Asn Gly Ala Gln Met Glu Lys Ile Pro Leu Leu His Ile Ser Ser Cys	
	405 410 415	
5	GAC CAA AAT ATT TCA GAA AAA GAC CTA TTA GAC ACA GAG AAC AAA AGA	1533
	Asp Gln Asn Ile Ser Glu Lys Asp Leu Leu Asp Thr Glu Asn Lys Arg	
	420 425 430 435	
10	AAG AAA GAT TTT CTT ACT TCA GAG AAT TCT TTG CCA CGT ATT TCT AGC	1581
	Lys Lys Asp Phe Leu Thr Ser Glu Asn Ser Leu Pro Arg Ile Ser Ser	
	440 445 450	
15	CTA CCA AAA TCA GAG AAG CCA TTA AAT GAG GAA ACA GTG GTA AAT AAG	1629
	Leu Pro Lys Ser Glu Lys Pro Leu Asn Glu Glu Thr Val Val Asn Lys	
	455 460 465	
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	470 475 480	
25	GTA AAG CAG GCA ATA TCT GGA ACT TCT CCA GTG GCT TCT TCA TTT CAG	1725
	Val Lys Gln Ala Ile Ser Gly Thr Ser Pro Val Ala Ser Ser Phe Gln	
	485 490 495	
30	GGT ATC AAA AAG TCT ATA TTC AGA ATA AGA GAA TCA CCT AAA GAG ACT	1773
	Gly Ile Lys Lys Ser Ile Phe Arg Ile Arg Glu Ser Pro Lys Glu Thr	
	500 505 510 515	
35	TTC AAT GCA AGT TTT TCA GGT CAT ATG ACT GAT CCA AAC TTT AAA AAA	1821
	Phe Asn Ala Ser Phe Ser Gly His Met Thr Asp Pro Asn Phe Lys Lys	
	520 525 530	
40	GAA ACT GAA GCC TCT GAA AGT GGA CTG GAA ATA CAT ACT GTT TGC TCA	1869
	Glu Thr Glu Ala Ser Glu Ser Gly Leu Glu Ile His Thr Val Cys Ser	
	535 540 545	
45	CAG AAG GAG GAC TCC TTA TGT CCA AAT TTA ATT GAT AAT GGA AGC TGG	1917
	Gln Lys Glu Asp Ser Leu Cys Pro Asn Leu Ile Asp Asn Gly Ser Trp	
	550 555 560	
50	CCA GCC ACC ACC ACA CAG AAT TCT GTA GCT TTG AAG AAT GCA GGT TTA	1965
	Pro Ala Thr Thr Thr Gln Asn Ser Val Ala Leu Lys Asn Ala Gly Leu	
	565 570 575	
55	ATA TCC ACT TTG AAA AAG AAA ACA AAT AAG TTT ATT TAT GCT ATA CAT	2013
	Ile Ser Thr Leu Lys Lys Lys Thr Asn Lys Phe Ile Tyr Ala Ile His	
	580 585 590 595	
60	GAT GAA ACA TCT TAT AAA GGA AAA AAA ATA CCG AAA GAC CAA AAA TCA	2061
	Asp Glu Thr Ser Tyr Lys Gly Lys Lys Ile Pro Lys Asp Gln Lys Ser	
	600 605 610	
65	GAA CTA ATT AAC TGT TCA GCC CAG TTT GAA GCA AAT GCT TTT GAA GCA	2109
	Glu Leu Ile Asn Cys Ser Ala Gln Phe Glu Ala Asn Ala Phe Glu Ala	
	615 620 625	
70	CCA CTT ACA TTT GCA AAT GCT GAT TCA GGT TTA TTG CAT TCT TCT GTG	2157
	Pro Leu Thr Phe Ala Asn Ala Asp Ser Gly Leu Leu His Ser Ser Val	
	630 635 640	
75	AAA AGA AGC TGT TCA CAG AAT GAT TCT GAA GAA CCA ACT TTG TCC TTA	2205

	Lys	Arg	Ser	Cys	Ser	Gln	Asn	Asp	Ser	Glu	Glu	Pro	Thr	Leu	Ser	Leu	
	645						650					655					
5	ACT	AGC	TCT	TTT	GGG	ACA	ATT	CTG	AGG	AAA	TGT	TCT	AGA	AAT	GAA	ACA	2253
	Thr	Ser	Ser	Phe	Gly	Thr	Ile	Leu	Arg	Lys	Cys	Ser	Arg	Asn	Glu	Thr	
	660					665					670				675		
10	TGT	TCT	AAT	AAT	ACA	GTA	ATC	TCT	CAG	GAT	CTT	GAT	TAT	AAA	GAA	GCA	2301
	Cys	Ser	Asn	Asn	Thr	Val	Ile	Ser	Gln	Asp	Leu	Asp	Tyr	Lys	Glu	Ala	
					680					685					690		
15	AAA	TGT	AAT	AAG	GAA	AAA	CTA	CAG	TTA	TTT	ATT	ACC	CCA	GAA	GCT	GAT	2349
	Lys	Cys	Asn	Lys	Glu	Lys	Leu	Gln	Leu	Phe	Ile	Thr	Pro	Glu	Ala	Asp	
				695					700					705			
20	TCT	CTG	TCA	TGC	CTG	CAG	GAA	GGA	CAG	TGT	GAA	AAT	GAT	CCA	AAA	AGC	2397
	Ser	Leu	Ser	Cys	Leu	Gln	Glu	Gly	Gln	Cys	Glu	Asn	Asp	Pro	Lys	Ser	
			710					715					720				
25	AAA	AAA	GTT	TCA	GAT	ATA	AAA	GAA	GAG	GTC	TTG	GCT	GCA	GCA	TGT	CAC	2445
	Lys	Lys	Val	Ser	Asp	Ile	Lys	Glu	Glu	Val	Leu	Ala	Ala	Ala	Cys	His	
			725				730					735					
30	CCA	GTA	CAA	CAT	TCA	AAA	GTG	GAA	TAC	AGT	GAT	ACT	GAC	TTT	CAA	TCC	2493
	Pro	Val	Gln	His	Ser	Lys	Val	Glu	Tyr	Ser	Asp	Thr	Asp	Phe	Gln	Ser	
						745					750				755		
35	CAG	AAA	AGT	CTT	TTA	TAT	GAT	CAT	GAA	AAT	GCC	AGC	ACT	CTT	ATT	TTA	2541
	Gln	Lys	Ser	Leu	Leu	Tyr	Asp	His	Glu	Asn	Ala	Ser	Thr	Leu	Ile	Leu	
					760					765					770		
40	ACT	CCT	ACT	TCC	AAG	GAT	GTT	CTG	TCA	AAC	CTA	GTC	ATG	ATT	TCT	AGA	2589
	Thr	Pro	Thr	Ser	Lys	Asp	Val	Leu	Ser	Asn	Leu	Val	Met	Ile	Ser	Arg	
				775				780						785			
45	GGC	AAA	GAA	TCA	TAC	AAA	ATG	TCA	GAC	AAG	CTC	AAA	GGT	AAC	AAT	TAT	2637
	Gly	Lys	Glu	Ser	Tyr	Lys	Met	Ser	Asp	Lys	Leu	Lys	Gly	Asn	Asn	Tyr	
			790					795					800				
50	GAA	TCT	GAT	GTT	GAA	TTA	ACC	AAA	AAT	ATT	CCC	ATG	GAA	AAG	AAT	CAA	2685
	Glu	Ser	Asp	Val	Glu	Leu	Thr	Lys	Asn	Ile	Pro	Met	Glu	Lys	Asn	Gln	
			805				810					815					
55	GAT	GTA	TGT	GCT	TTA	AAT	GAA	AAT	TAT	AAA	AAC	GTT	GAG	CTG	TTG	CCA	2733
	Asp	Val	Cys	Ala	Leu	Asn	Glu	Asn	Tyr	Lys	Asn	Val	Glu	Leu	Leu	Pro	
						825					830				835		
60	CCT	GAA	AAA	TAC	ATG	AGA	GTA	GCA	TCA	CCT	TCA	AGA	AAG	GTA	CAA	TTC	2781
	Pro	Glu	Lys	Tyr	Met	Arg	Val	Ala	Ser	Pro	Ser	Arg	Lys	Val	Gln	Phe	
					840					845					850		
65	AAC	CAA	AAC	ACA	AAT	CTA	AGA	GTA	ATC	CAA	AAA	AAT	CAA	GAA	GAA	ACT	2829
	Asn	Gln	Asn	Thr	Asn	Leu	Arg	Val	Ile	Gln	Lys	Asn	Gln	Glu	Glu	Thr	
				855					860					865			
70	ACT	TCA	ATT	TCA	AAA	ATA	ACT	GTC	AAT	CCA	GAC	TCT	GAA	GAA	CTT	TTC	2877
	Thr	Ser	Ile	Ser	Lys	Ile	Thr	Val	Asn	Pro	Asp	Ser	Glu	Glu	Leu	Phe	
			870					875					880				
75	TCA	GAC	AAT	GAG	AAT	AAT	TTT	GTC	TTC	CAA	GTA	GCT	AAT	GAA	AGG	AAT	2925
	Ser	Asp	Asn	Glu	Asn	Asn	Phe	Val	Phe	Gln	Val	Ala	Asn	Glu	Arg	Asn	

	885	890	895	
5	AAT CTT GCT TTA GGA AAT ACT AAG GAA CTT CAT GAA ACA GAC TTG ACT Asn Leu Ala Leu Gly Asn Thr Lys Glu Leu His Glu Thr Asp Leu Thr 900 905 910 915	2973		
10	TGT GTA AAC GAA CCC ATT TTC AAG AAC TCT ACC ATG GTT TTA TAT GGA Cys Val Asn Glu Pro Ile Phe Lys Asn Ser Thr Met Val Leu Tyr Gly 920 925 930	3021		
15	GAC ACA GGT GAT AAA CAA GCA ACC CAA GTG TCA ATT AAA AAA GAT TTG Asp Thr Gly Asp Lys Gln Ala Thr Gln Val Ser Ile Lys Lys Asp Leu 935 940 945	3069		
20	GTT TAT GTT CTT GCA GAG GAG AAC AAA AAT AGT GTA AAG CAG CAT ATA Val Tyr Val Leu Ala Glu Glu Asn Lys Asn Ser Val Lys Gln His Ile 950 955 960	3117		
25	AAA ATG ACT CTA GGT CAA GAT TTA AAA TCG GAC ATC TCC TTG AAT ATA Lys Met Thr Leu Gly Gln Asp Leu Lys Ser Asp Ile Ser Leu Asn Ile 965 970 975	3165		
30	GAT AAA ATA CCA GAA AAA AAT AAT GAT TAC ATG AAC AAA TGG GCA GGA Asp Lys Ile Pro Glu Lys Asn Asn Asp Tyr Met Asn Lys Trp Ala Gly 980 985 990 995	3213		
35	CTC TTA GGT CCA ATT TCA AAT CAC AGT TTT GGA GGT AGC TTC AGA ACA Leu Leu Gly Pro Ile Ser Asn His Ser Phe Gly Gly Ser Phe Arg Thr 1000 1005 1010	3261		
40	GCT TCA AAT AAG GAA ATC AAG CTC TCT GAA CAT AAC ATT AAG AAG AGC Ala Ser Asn Lys Glu Ile Lys Leu Ser Glu His Asn Ile Lys Lys Ser 1015 1020 1025	3309		
45	AAA ATG TTC TTC AAA GAT ATT GAA GAA CAA TAT CCT ACT AGT TTA GCT Lys Met Phe Phe Lys Asp Ile Glu Glu Gln Tyr Pro Thr Ser Leu Ala 1030 1035 1040	3357		
50	TGT GTT GAA ATT GAA AAT ACC TTG GCA TTA GAT AAT CAA AAG AAA CTG Cys Val Glu Ile Val Asn Thr Leu Ala Leu Asp Asn Gln Lys Lys Leu 1045 1050 1055	3405		
55	AGC AAG CCT CAG TCA ATT AAT ACT GTA TCT GCA CAT TTA CAG AGT AGT Ser Lys Pro Gln Ser Ile Asn Thr Val Ser Ala His Leu Gln Ser Ser 1060 1065 1070 1075	3453		
60	GTA GTT GTT TCT GAT TGT AAA AAT AGT CAT ATA ACC CCT CAG ATG TTA Val Val Val Ser Asp Cys Lys Asn Ser His Ile Thr Pro Gln Met Leu 1080 1085 1090	3501		
65	TTT TCC AAG CAG GAT TTT AAT TCA AAC CAT AAT TTA ACA CCT AGC CAA Phe Ser Lys Gln Asp Phe Asn Ser Asn His Asn Leu Thr Pro Ser Gln 1095 1100 1105	3549		
70	AAG GCA GAA ATT ACA GAA CTT TCT ACT ATA TTA GAA GAA TCA GGA AGT Lys Ala Glu Ile Thr Glu Leu Ser Thr Ile Leu Glu Glu Ser Gly Ser 1110 1115 1120	3597		
75	CAG TTT GAA TTT ACT CAG TTT AGA AAA CCA AGC TAC ATA TTG CAG AAG Gln Phe Glu Phe Thr Gln Phe Arg Lys Pro Ser Tyr Ile Leu Gln Lys 1125 1130 1135	3645		



	AGT ACA TTT GAA GTG CCT GAA AAC CAG ATG ACT ATC TTA AAG ACC ACT	3693
5	Ser Thr Phe Glu Val Pro Glu Asn Gln Met Thr Ile Leu Lys Thr Thr	
	1140 1145 1150 1155	
	TCT GAG GAA TGC AGA GAT GCT GAT CTT CAT GTC ATA ATG AAT GCC CCA	3741
	Ser Glu Glu Cys Arg Asp Ala Asp Leu His Val Ile Met Asn Ala Pro	
	1160 1165 1170	
10	TCG ATT GGT CAG GTA GAC AGC AGC AAG CAA TTT GAA GGT ACA GTT GAA	3789
	Ser Ile Gly Gln Val Asp Ser Ser Lys Gln Phe Glu Gly Thr Val Glu	
	1175 1180 1185	
15	ATT AAA CGG AAG TTT GCT GGC CTG TTG AAA AAT GAC TGT AAC AAA AGT	3837
	Ile Lys Arg Lys Phe Ala Gly Leu Leu Lys Asn Asp Cys Asn Lys Ser	
	1190 1195 1200	
20	GCT TCT GGT TAT TTA ACA GAT GAA AAT GAA GTG GGG TTT AGG GGC TTT	3885
	Ala Ser Gly Tyr Leu Thr Asp Glu Asn Glu Val Gly Phe Arg Gly Phe	
	1205 1210 1215	
25	TAT TCT GCT CAT GGC ACA AAA CTG AAT GTT TCT ACT GAA GCT CTG CAA	3933
	Tyr Ser Ala His Gly Thr Lys Leu Asn Val Ser Thr Glu Ala Leu Gln	
	1220 1225 1230 1235	
30	AAA GCT GTG AAA CTG TTT AGT GAT ATT GAG AAT ATT AGT GAG GAA ACT	3981
	Lys Ala Val Lys Leu Phe Ser Asp Ile Glu Asn Ile Ser Glu Glu Thr	
	1240 1245 1250	
35	TCT GCA GAG GTA CAT CCA ATA AGT TTA TCT TCA AGT AAA TGT CAT GAT	4029
	Ser Ala Glu Val His Pro Ile Ser Leu Ser Ser Ser Lys Cys His Asp	
	1255 1260 1265	
40	TCT GTT GTT TCA ATG TTT AAG ATA GAA AAT CAT AAT GAT AAA ACT GTA	4077
	Ser Val Val Ser Met Phe Lys Ile Glu Asn His Asn Asp Lys Thr Val	
	1270 1275 1280	
45	AGT GAA AAA AAT AAT AAA TGC CAA CTG ATA TTA CAA AAT AAT ATT GAA	4125
	Ser Glu Lys Asn Asn Lys Cys Gln Leu Ile Leu Gln Asn Asn Ile Glu	
	1285 1290 1295	
50	ATG ACT ACT GGC ACT TTT GTT GAA GAA ATT ACT GAA AAT TAC AAG AGA	4173
	Met Thr Thr Gly Thr Phe Val Glu Glu Ile Thr Glu Asn Tyr Lys Arg	
	1300 1305 1310 1315	
55	AAT ACT GAA AAT GAA GAT AAC AAA TAT ACT GCT GCC AGT AGA AAT TCT	4221
	Asn Thr Glu Asn Glu Asp Asn Lys Tyr Thr Ala Ala Ser Arg Asn Ser	
	1320 1325 1330	
60	CAT AAC TTA GAA TTT GAT GGC AGT GAT TCA AGT AAA AAT GAT ACT GTT	4269
	His Asn Leu Glu Phe Asp Gly Ser Asp Ser Ser Lys Asn Asp Thr Val	
	1335 1340 1345	
65	TGT ATT CAT AAA GAT GAA ACG GAC TTG CTA TTT ACT GAT CAG CAC AAC	4317
	Cys Ile His Lys Asp Glu Thr Asp Leu Leu Phe Thr Asp Gln His Asn	
	1350 1355 1360	
70	ATA TGT CTT AAA TTA TCT GGC CAG TTT ATG AAG GAG GGA AAC ACT CAG	4365
	Ile Cys Leu Lys Leu Ser Gly Gln Phe Met Lys Glu Gly Asn Thr Gln	
	1365 1370 1375	

	ATT AAA GAA GAT TTG TCA GAT TTA ACT TTT TTG GAA GTT GCG AAA GCT	4413
	Ile Lys Glu Asp Leu Ser Asp Leu Thr Phe Leu Glu Val Ala Lys Ala	
	1380 1385 1390 1395	
5	CAA GAA GCA TGT CAT GGT AAT ACT TCA AAT AAA GAA CAG TTA ACT GCT	4461
	Gln Glu Ala Cys His Gly Asn Thr Ser Asn Lys Glu Gln Leu Thr Ala	
	1400 1405 1410	
10	ACT AAA ACG GAG CAA AAT ATA AAA GAT TTT GAG ACT TCT GAT ACA TTT	4509
	Thr Lys Thr Glu Gln Asn Ile Lys Asp Phe Glu Thr Ser Asp Thr Phe	
	1415 1420 1425	
15	TTT CAG ACT GCA AGT GGG AAA AAT ATT AGT GTC GCC AAA GAG TCA TTT	4557
	Phe Gln Thr Ala Ser Gly Lys Asn Ile Ser Val Ala Lys Glu Ser Phe	
	1430 1435 1440	
20	AAT AAA ATT GTA AAT TTC TTT GAT CAG AAA CCA GAA GAA TTG CAT AAC	4605
	Asn Lys Ile Val Asn Phe Phe Asp Gln Lys Pro Glu Glu Leu His Asn	
	1445 1450 1455	
25	TTT TCC TTA AAT TCT GAA TTA CAT TCT GAC ATA AGA AAG AAC AAA ATG	4653
	Phe Ser Leu Asn Ser Glu Leu His Ser Asp Ile Arg Lys Asn Lys Met	
	1460 1465 1470 1475	
30	GAC ATT CTA AGT TAT GAG GAA ACA GAC ATA GTT AAA CAC AAA ATA CTG	4701
	Asp Ile Leu Ser Tyr Glu Glu Thr Asp Ile Val Lys His Lys Ile Leu	
	1480 1485 1490	
35	AAA GAA AGT GTC CCA GTT GGT ACT GGA AAT CAA CTA GTG ACC TTC CAG	4749
	Lys Glu Ser Val Pro Val Gly Thr Gly Asn Gln Leu Val Thr Phe Gln	
	1495 1500 1505	
40	GGA CAA CCC GAA CGT GAT GAA AAG ATC AAA GAA CCT ACT CTG TTG GGT	4797
	Gly Gln Pro Glu Arg Asp Glu Lys Ile Lys Glu Pro Thr Leu Leu Gly	
	1510 1515 1520	
45	TTT CAT ACA GCT AGC GGG AAA AAA GTT AAA ATT GCA AAG GAA TCT TTG	4845
	Phe His Thr Ala Ser Gly Lys Lys Val Lys Ile Ala Lys Glu Ser Leu	
	1525 1530 1535	
50	GAC AAA GTG AAA AAC CTT TTT GAT GAA AAA GAG CAA GGT ACT AGT GAA	4893
	Asp Lys Val Lys Asn Leu Phe Asp Glu Lys Glu Gln Gly Thr Ser Glu	
	1540 1545 1550 1555	
55	ATC ACC AGT TTT AGC CAT CAA TGG GCA AAG ACC CTA AAG TAC AGA GAG	4941
	Ile Thr Ser Phe Ser His Gln Trp Ala Lys Thr Leu Lys Tyr Arg Glu	
	1560 1565 1570	
60	GCC TGT AAA GAC CTT GAA TTA GCA TGT GAG ACC ATT GAG ATC ACA GCT	4989
	Ala Cys Lys Asp Leu Glu Leu Ala Cys Glu Thr Ile Glu Ile Thr Ala	
	1575 1580 1585	
65	GCC CCA AAG TGT AAA GAA ATG CAG AAT TCT CTC AAT AAT GAT AAA AAC	5037
	Ala Pro Lys Cys Lys Glu Met Gln Asn Ser Leu Asn Asn Asp Lys Asn	
	1590 1595 1600	
70	CTT GTT TCT ATT GAG ACT GTG GTG CCA CCT AAG CTC TTA AGT GAT AAT	5085
	Leu Val Ser Ile Glu Thr Val Val Pro Pro Lys Leu Leu Ser Asp Asn	
	1605 1610 1615	
75	TTA TGT AGA CAA ACT GAA AAT CTC AAA ACA TCA AAA AGT ATC TTT TTG	5133

	Leu Cys Arg Gln Thr Glu Asn Leu Lys Thr Ser Lys Ser Ile Phe Leu	
	1620 1625 1630 1635	
5	AAA GTT AAA GTA CAT GAA AAT GTA GAA AAA GAA ACA GCA AAA AGT CCT Lys Val Lys Val His Glu Asn Val Glu Lys Glu Thr Ala Lys Ser Pro	5181
	1640 1645 1650	
10	GCA ACT TGT TAC ACA AAT CAG TCC CCT TAT TCA GTC ATT GAA AAT TCA Ala Thr Cys Tyr Thr Asn Gln Ser Pro Tyr Ser Val Ile Glu Asn Ser	5229
	1655 1660 1665	
15	GCC TTA GCT TTT TAC ACA AGT TGT AGT AGA AAA ACT TCT GTG AGT CAG Ala Leu Ala Phe Tyr Thr Ser Cys Ser Arg Lys Thr Ser Val Ser Gln	5277
	1670 1675 1680	
20	ACT TCA TTA CTT GAA GCA AAA AAA TGG CTT AGA GAA GGA ATA TTT GAT Thr Ser Leu Leu Glu Ala Lys Lys Trp Leu Arg Glu Gly Ile Phe Asp	5325
	1685 1690 1695	
25	GGT CAA CCA GAA AGA ATA AAT ACT GCA GAT TAT GTA GGA AAT TAT TTG Gly Gln Pro Glu Arg Ile Asn Thr Ala Asp Tyr Val Gly Asn Tyr Leu	5373
	1700 1705 1710 1715	
30	TAT GAA AAT AAT TCA AAC AGT ACT ATA GCT GAA AAT GAC AAA AAT CAT Tyr Glu Asn Asn Ser Asn Ser Thr Ile Ala Glu Asn Asp Lys Asn His	5421
	1720 1725 1730	
35	CTC TCC GAA AAA CAA GAT ACT TAT TTA AGT AAC AGT AGC ATG TCT AAC Leu Ser Glu Lys Gln Asp Thr Tyr Leu Ser Asn Ser Ser Met Ser Asn	5469
	1735 1740 1745	
40	AGC TAT TCC TAC CAT TCT GAT GAG GTA TAT AAT GAT TCA GGA TAT CTC Ser Tyr Ser Tyr His Ser Asp Glu Val Tyr Asn Asp Ser Gly Tyr Leu	5517
	1750 1755 1760	
45	TCA AAA AAT AAA CTT GAT TCT GGT ATT GAG CCA GTA TTG AAG AAT GTT Ser Lys Asn Lys Leu Asp Ser Gly Ile Glu Pro Val Leu Lys Asn Val	5565
	1765 1770 1775	
50	GAA GAT CAA AAA AAC ACT AGT TTT TCC AAA GTA ATA TCC AAT GTA AAA Glu Asp Gln Lys Asn Thr Ser Phe Ser Lys Val Ile Ser Asn Val Lys	5613
	1780 1785 1790 1795	
55	GAT GCA AAT GCA TAC CCA CAA ACT GTA AAT GAA GAT ATT TGC GTT GAG Asp Ala Asn Ala Tyr Pro Gln Thr Val Asn Glu Asp Ile Cys Val Glu	5661
	1800 1805 1810	
60	GAA CTT GTG ACT AGC TCT TCA CCC TGC AAA AAT AAA AAT GCA GCC ATT Glu Leu Val Thr Ser Ser Pro Cys Lys Asn Lys Asn Ala Ala Ile	5709
	1815 1820 1825	
65	AAA TTG TCC ATA TCT AAT AGT AAT AAT TTT GAG GTA GGG CCA CCT GCA Lys Leu Ser Ile Ser Asn Ser Asn Asn Phe Glu Val Gly Pro Pro Ala	5757
	1830 1835 1840	
70	TTT AGG ATA GCC AGT GGT AAA ATC GTT TGT GTT TCA CAT GAA ACA ATT Phe Arg Ile Ala Ser Gly Lys Ile Val Cys Val Ser His Glu Thr Ile	5805
	1845 1850 1855	
75	AAA AAA GTG AAA GAC ATA TTT ACA GAC AGT TTC AGT AAA GTA ATT AAG Lys Lys Val Lys Asp Ile Phe Thr Asp Ser Phe Ser Lys Val Ile Lys	5853

	1860	1865	1870	1875	
5	GAA AAC AAC GAG AAT AAA TCA AAA ATT TGC CAA ACG AAA ATT ATG GCA Glu Asn Asn Glu Asn Lys Ser Lys Ile Cys Gln Thr Lys Ile Met Ala	1880	1885	1890	5901
10	GGT TGT TAC GAG GCA TTG GAT GAT TCA GAG GAT ATT CTT CAT AAC TCT Gly Cys Tyr Glu Ala Leu Asp Asp Ser Glu Asp Ile Leu His Asn Ser	1895	1900	1905	5949
15	CTA GAT AAT GAT GAA TGT AGC ACG CAT TCA CAT AAG GTT TTT GCT GAC Leu Asp Asn Asp Glu Cys Ser Thr His Ser His Lys Val Phe Ala Asp	1910	1915	1920	5997
20	ATT CAG AGT GAA GAA ATT TTA CAA CAT AAC CAA AAT ATG TCT GGA TTG Ile Gln Ser Glu Glu Ile Leu Gln His Asn Gln Asn Met Ser Gly Leu	1925	1930	1935	6045
25	GAG AAA GTT TCT AAA ATA TCA CCT TGT GAT GTT AGT TTG GAA ACT TCA Glu Lys Val Ser Lys Ile Ser Pro Cys Asp Val Ser Leu Glu Thr Ser	1940	1945	1950	6093
30	GAT ATA TGT AAA TGT AGT ATA GGG AAG CTT CAT AAG TCA GTC TCA TCT Asp Ile Cys Lys Cys Ser Ile Gly Lys Leu His Lys Ser Val Ser Ser	1960	1965	1970	6141
35	GCA AAT ACT TGT GGG ATT TTT AGC ACA GCA AGT GGA AAA TCT GTC CAG Ala Asn Thr Cys Gly Ile Phe Ser Thr Ala Ser Gly Lys Ser Val Gln	1975	1980	1985	6189
40	GTA TCA GAT GCT TCA TTA CAA AAC GCA AGA CAA GTG TTT TCT GAA ATA Val Ser Asp Ala Ser Leu Gln Asn Ala Arg Gln Val Phe Ser Glu Ile	1990	1995	2000	6237
45	GAA GAT AGT ACC AAG CAA GTC TTT TCC AAA GTA TTG TTT AAA AGT AAC Glu Asp Ser Thr Lys Gln Val Phe Ser Lys Val Leu Phe Lys Ser Asn	2005	2010	2015	6285
50	GAA CAT TCA GAC CAG CTC ACA AGA GAA GAA AAT ACT GCT ATA CGT ACT Glu His Ser Asp Gln Leu Thr Arg Glu Glu Asn Thr Ala Ile Arg Thr	2020	2025	2030	6333
55	CCA GAA CAT TTA ATA TCC CAA AAA GGC TTT TCA TAT AAT GTG GTA AAT Pro Glu His Leu Ile Ser Gln Lys Gly Phe Ser Tyr Asn Val Val Asn	2040	2045	2050	6381
60	TCA TCT GCT TTC TCT GGA TTT AGT ACA GCA AGT GGA AAG CAA GTT TCC Ser Ser Ala Phe Ser Gly Phe Ser Thr Ala Ser Gly Lys Gln Val Ser	2055	2060	2065	6429
	ATT TTA GAA AGT TCC TTA CAC AAA GTT AAG GGA GTG TTA GAG GAA TTT Ile Leu Glu Ser Ser Leu His Lys Val Lys Gly Val Leu Glu Glu Phe	2070	2075	2080	6477
	GAT TTA ATC AGA ACT GAG CAT AGT CTT CAC TAT TCA CCT ACG TCT AGA Asp Leu Ile Arg Thr Glu His Ser Leu His Tyr Ser Pro Thr Ser Arg	2085	2090	2095	6525
	CAA AAT GTA TCA AAA ATA CTT CCT CGT GTT GAT AAG AGA AAC CCA GAG Gln Asn Val Ser Lys Ile Leu Pro Arg Val Asp Lys Arg Asn Pro Glu	2100	2105	2110	6573

5	CAC TGT GTA AAC TCA GAA ATG GAA AAA ACC TGC AGT AAA GAA TTT AAA His Cys Val Asn Ser Glu Met Glu Lys Thr Cys Ser Lys Glu Phe Lys 2120 2125 2130	6621
10	TTA TCA AAT AAC TTA AAT GTT GAA GGT GGT TCT TCA GAA AAT AAT CAC Leu Ser Asn Asn Leu Asn Val Glu Gly Gly Ser Ser Glu Asn Asn His 2135 2140 2145	6669
15	TCT ATT AAA GTT TCT CCA TAT CTC TCT CAA TTT CAA CAA GAC AAA CAA Ser Ile Lys Val Ser Pro Tyr Leu Ser Gln Phe Gln Gln Asp Lys Gln 2150 2155 2160	6717
20	CAG TTG GTA TTA GGA ACC AAA GTC TCA CTT GTT GAG AAC ATT CAT GTT Gln Leu Val Leu Gly Thr Lys Val Ser Leu Val Glu Asn Ile His Val 2165 2170 2175	6765
25	TTG GGA AAA GAA CAG GCT TCA CCT AAA AAC GTA AAA ATG GAA ATT GGT Leu Gly Lys Glu Gln Ala Ser Pro Lys Asn Val Lys Met Glu Ile Gly 2180 2185 2190 2195	6813
30	AAA ACT GAA ACT TTT TCT GAT GTT CCT GTG AAA ACA AAT ATA GAA GTT Lys Thr Glu Thr Phe Ser Asp Val Pro Val Lys Thr Asn Ile Glu Val 2200 2205 2210	6861
35	TGT TCT ACT TAC TCC AAA GAT TCA GAA AAC TAC TTT GAA ACA GAA GCA Cys Ser Thr Tyr Ser Lys Asp Ser Glu Asn Tyr Phe Glu Thr Glu Ala 2215 2220 2225	6909
40	GTA GAA ATT GCT AAA GCT TTT ATG GAA GAT GAT GAA CTG ACA GAT TCT Val Glu Ile Ala Lys Ala Phe Met Glu Asp Asp Glu Leu Thr Asp Ser 2230 2235 2240	6957
45	AAA CTG CCA AGT CAT GCC ACA CAT TCT CTT TTT ACA TGT CCC GAA AAT Lys Leu Pro Ser His Ala Thr His Ser Leu Phe Thr Cys Pro Glu Asn 2245 2250 2255	7005
50	GAG GAA ATG GTT TCG TCA AAT TCA AGA ATT GGA AAA AGA AGA GGA GAG Glu Glu Met Val Leu Ser Asn Ser Arg Ile Gly Lys Arg Arg Gly Glu 2260 2265 2270 2275	7053
55	CCC CTT ATC TTA GTG GGA GAA CCC TCA ATC AAA AGA AAC TTA TTA AAT Pro Leu Ile Leu Val Gly Glu Pro Ser Ile Lys Arg Asn Leu Leu Asn 2280 2285 2290	7101
60	GAA TTT GAC AGG ATA ATA GAA AAT CAA GAA AAA TCC TTA AAG GCT TCA Glu Phe Asp Arg Ile Ile Glu Asn Gln Glu Lys Ser Leu Lys Ala Ser 2295 2300 2305	7149
65	AAA AGC ACT CCA GAT GGC ACA ATA AAA GAT CGA AGA TTG TTT ATG CAT Lys Ser Thr Pro Asp Gly Thr Ile Lys Asp Arg Arg Leu Phe Met His 2310 2315 2320	7197
70	CAT GTT TCT TTA GAG CCG ATT ACC TGT GTA CCC TTT CGC ACA ACT AAG His Val Ser Leu Glu Pro Ile Thr Cys Val Pro Phe Arg Thr Thr Lys 2325 2330 2335	7245
75	GAA CGT CAA GAG ATA CAG AAT CCA AAT TTT ACC GCA CCT GGT CAA GAA Glu Arg Gln Glu Ile Gln Asn Pro Asn Phe Thr Ala Pro Gly Gln Glu 2340 2345 2350 2355	7293

	TTT CTG TCT AAA TCT CAT TTG TAT GAA CAT CTG ACT TTG GAA AAA TCT	7341
	Phe Leu Ser Lys Ser His Leu Tyr Glu His Leu Thr Leu Glu Lys Ser	
	2360 2365 2370	
5	TCA AGC AAT TTA GCA GTT TCA GGA CAT CCA TTT TAT CAA GTT TCT GCT	7389
	Ser Ser Asn Leu Ala Val Ser Gly His Pro Phe Tyr Gln Val Ser Ala	
	2375 2380 2385	
10	ACA AGA AAT GAA AAA ATG AGA CAC TTG ATT ACT ACA GGC AGA CCA ACC	7437
	Thr Arg Asn Glu Lys Met Arg His Leu Ile Thr Thr Gly Arg Pro Thr	
	2390 2395 2400	
15	AAA GTC TTT GTT CCA CCT TTT AAA ACT AAA TCA CAT TTT CAC AGA GTT	7485
	Lys Val Phe Val Pro Pro Phe Lys Thr Lys Ser His Phe His Arg Val	
	2405 2410 2415	
20	GAA CAG TGT GTT AGG AAT ATT AAC TTG GAG GAA AAC AGA CAA AAG CAA	7533
	Glu Gln Cys Val Arg Asn Ile Asn Leu Glu Glu Asn Arg Gln Lys Gln	
	2420 2425 2430 2435	
	AAC ATT GAT GGA CAT GGC TCT GAT GAT AGT AAA AAT AAG ATT AAT GAC	7581
	Asn Ile Asp Gly His Gly Ser Asp Asp Ser Lys Asn Lys Ile Asn Asp	
	2440 2445 2450	
25	AAT GAG ATT CAT CAG TTT AAC AAA AAC AAC TCC AAT CAA GCA GCA GCT	7629
	Asn Glu Ile His Gln Phe Asn Lys Asn Asn Ser Asn Gln Ala Ala Ala	
	2455 2460 2465	
30	GTA ACT TTC ACA AAG TGT GAA GAA GAA CCT TTA GAT TTA ATT ACA AGT	7677
	Val Thr Phe Thr Lys Cys Glu Glu Glu Pro Leu Asp Leu Ile Thr Ser	
	2470 2475 2480	
35	CTT CAG AAT GCC AGA GAT ATA CAG GAT ATG CGA ATT AAG AAG AAA CAA	7725
	Leu Gln Asn Ala Arg Asp Ile Gln Asp Met Arg Ile Lys Lys Lys Gln	
	2485 2490 2495	
40	AGG CAA CGC GTC TTT CCA CAG CCA GGC AGT CTG TAT CTT GCA AAA ACA	7773
	Arg Gln Arg Val Phe Pro Gln Pro Gly Ser Leu Tyr Leu Ala Lys Thr	
	2500 2505 2510 2515	
	TCC ACT CTG CCT CGA ATC TCT CTG AAA GCA GCA GTA GGA GGC CAA GTT	7821
	Ser Thr Leu Pro Arg Ile Ser Leu Lys Ala Ala Val Gly Gly Gln Val	
	2520 2525 2530	
45	CCC TCT GCG TGT TCT CAT AAA CAG CTG TAT ACG TAT GGC GTT TCT AAA	7869
	Pro Ser Ala Cys Ser His Lys Gln Leu Tyr Thr Tyr Gly Val Ser Lys	
	2535 2540 2545	
50	CAT TGC ATA AAA ATT AAC AGC AAA AAT GCA GAG TCT TTT CAG TTT CAC	7917
	His Cys Ile Lys Ile Asn Ser Lys Asn Ala Glu Ser Phe Gln Phe His	
	2550 2555 2560	
55	ACT GAA GAT TAT TTT GGT AAG GAA AGT TTA TGG ACT GGA AAA GGA ATA	7965
	Thr Glu Asp Tyr Phe Gly Lys Glu Ser Leu Trp Thr Gly Lys Gly Ile	
	2565 2570 2575	
60	CAG TTG GCT GAT GGT GGA TGG CTC ATA CCC TCC AAT GAT GGA AAG GCT	8013
	Gln Leu Ala Asp Gly Gly Trp Leu Ile Pro Ser Asn Asp Gly Lys Ala	
	2580 2585 2590 2595	
	GGA AAA GAA GAA TTT TAT AGG GCT CTG TGT GAC ACT CCA GGT GTG GAT	8061

	Gly	Lys	Glu	Glu	Phe	Tyr	Arg	Ala	Leu	Cys	Asp	Thr	Pro	Gly	Val	Asp	
					2600					2605					2610		
5	CCA	AAG	CTT	ATT	TCT	AGA	ATT	TGG	GTT	TAT	AAT	CAC	TAT	AGA	TGG	ATC	8109
	Pro	Lys	Leu	Ile	Ser	Arg	Ile	Trp	Val	Tyr	Asn	His	Tyr	Arg	Trp	Ile	
					2615					2620					2625		
10	ATA	TGG	AAA	CTG	GCA	GCT	ATG	GAA	TGT	GCC	TTT	CCT	AAG	GAA	TTT	GCT	8157
	Ile	Trp	Lys	Leu	Ala	Ala	Met	Glu	Cys	Ala	Phe	Pro	Lys	Glu	Phe	Ala	
					2630					2635					2640		
15	AAT	AGA	TGC	CTA	AGC	CCA	GAA	AGG	GTG	CTT	CTT	CAA	CTA	AAA	TAC	AGA	8205
	Asn	Arg	Cys	Leu	Ser	Pro	Glu	Arg	Val	Leu	Leu	Gln	Leu	Lys	Tyr	Arg	
					2645					2650					2655		
20	TAT	GAT	ACG	GAA	ATT	GAT	AGA	AGC	AGA	AGA	TCG	GCT	ATA	AAA	AAG	ATA	8253
	Tyr	Asp	Thr	Glu	Ile	Asp	Arg	Ser	Arg	Arg	Ser	Ala	Ile	Lys	Lys	Ile	
	2660					2665					2670					2675	
	ATG	GAA	AGG	GAT	GAC	ACA	GCT	GCA	AAA	ACA	CTT	GTT	CTC	TGT	GTT	TCT	8301
	Met	Glu	Arg	Asp	Asp	Thr	Ala	Ala	Lys	Thr	Leu	Val	Leu	Cys	Val	Ser	
					2680						2685					2690	
25	GAC	ATA	ATT	TCA	TTG	AGC	GCA	AAT	ATA	TCT	GAA	ACT	TCT	AGC	AAT	AAA	8349
	Asp	Ile	Ile	Ser	Leu	Ser	Ala	Asn	Ile	Ser	Glu	Thr	Ser	Ser	Asn	Lys	
					2695					2700						2705	
30	ACT	AGT	AGT	GCA	GAT	ACC	CAA	AAA	GTG	GCC	ATT	ATT	GAA	CTT	ACA	GAT	8397
	Thr	Ser	Ser	Ala	Asp	Thr	Gln	Lys	Val	Ala	Ile	Ile	Glu	Leu	Thr	Asp	
					2710					2715					2720		
35	GGG	TGG	TAT	GCT	GTT	AAG	GCC	CAG	TTA	GAT	CCT	CCC	CTC	TTA	GCT	GTC	8445
	Gly	Trp	Tyr	Ala	Val	Lys	Ala	Gln	Leu	Asp	Pro	Pro	Leu	Leu	Ala	Val	
					2725					2730					2735		
40	TTA	AAG	AAT	GGC	AGA	CTG	ACA	GTT	GGT	CAG	AAG	ATT	ATT	CTT	CAT	GGA	8493
	Leu	Lys	Asn	Gly	Arg	Leu	Thr	Val	Gly	Gln	Lys	Ile	Ile	Leu	His	Gly	
	2740					2745					2750					2755	
	GCA	GAA	CTG	GTG	GGC	TCT	CCT	GAT	GCC	TGT	ACA	CCT	CTT	GAA	GCC	CCA	8541
	Ala	Glu	Leu	Val	Gly	Ser	Pro	Asp	Ala	Cys	Thr	Pro	Leu	Glu	Ala	Pro	
					2760						2765					2770	
45	GAA	TCT	CTT	ATG	TTA	AAG	ATT	TCT	GCT	AAC	AGT	ACT	CGG	CCT	GCT	CGC	8589
	Glu	Ser	Leu	Met	Leu	Lys	Ile	Ser	Ala	Asn	Ser	Thr	Arg	Pro	Ala	Arg	
					2775					2780						2785	
50	TGG	TAT	ACC	AAA	CTT	GGA	TTC	TTT	CCT	GAC	CCT	AGA	CCT	TTT	CCT	CTG	8637
	Trp	Tyr	Thr	Lys	Leu	Gly	Phe	Phe	Pro	Asp	Pro	Arg	Pro	Phe	Pro	Leu	
					2790					2795					2800		
55	CCC	TTA	TCA	TCG	CTT	TTC	AGT	GAT	GGA	GGA	AAT	GTT	GGT	TGT	GTT	GAT	8685
	Pro	Leu	Ser	Ser	Leu	Phe	Ser	Asp	Gly	Gly	Asn	Val	Gly	Cys	Val	Asp	
					2805					2810					2815		
60	GTA	ATT	ATT	CAA	AGA	GCA	TAC	CCT	ATA	CAG	TGG	ATG	GAG	AAG	ACA	TCA	8733
	Val	Ile	Ile	Gln	Arg	Ala	Tyr	Pro	Ile	Gln	Trp	Met	Glu	Lys	Thr	Ser	
	2820					2825					2830					2835	
	TCT	GGA	TTA	TAC	ATA	TTT	CGC	AAT	GAA	AGA	GAG	GAA	GAA	AAG	GAA	GCA	8781
	Ser	Gly	Leu	Tyr	Ile	Phe	Arg	Asn	Glu	Arg	Glu	Glu	Glu	Lys	Glu	Ala	

	2840	2845	2850	
5	GCA AAA TAT GTG GAG GCC CAA CAA AAG AGA CTA GAA GCC TTA TTC ACT Ala Lys Tyr Val Glu Ala Gln Gln Lys Arg Leu Glu Ala Leu Phe Thr 2855 2860 2865	8829		
10	AAA ATT CAG GAG GAA TTT GAA GAA CAT GAA GAA AAC ACA ACA AAA CCA Lys Ile Gln Glu Glu Phe Glu Glu His Glu Glu Asn Thr Thr Lys Pro 2870 2875 2880	8877		
15	TAT TTA CCA TCA CGT GCA CTA ACA AGA CAG CAA GTT CGT GCT TTG CAA Tyr Leu Pro Ser Arg Ala Leu Thr Arg Gln Gln Val Arg Ala Leu Gln 2885 2890 2895	8925		
	GAT GGT GCA GAG CTT TAT GAA GCA GTG AAG AAT GCA GCA GAC CCA GCT Asp Gly Ala Glu Leu Tyr Glu Ala Val Lys Asn Ala Ala Asp Pro Ala 2900 2905 2910 2915	8973		
20	TAC CTT GAG GGT TAT TTC AGT GAA GAG CAG TTA AGA GCC TTG AAT AAT Tyr Leu Glu Gly Tyr Phe Ser Glu Glu Gln Leu Arg Ala Leu Asn Asn 2920 2925 2930	9021		
25	CAC AGG CAA ATG TTG AAT GAT AAG AAA CAA GCT CAG ATC CAG TTG GAA His Arg Gln Met Leu Asn Asp Lys Lys Gln Ala Gln Ile Gln Leu Glu 2935 2940 2945	9069		
30	ATT AGG AAG GCC ATG GAA TCT GCT GAA CAA AAG GAA CAA GGT TTA TCA Ile Arg Lys Ala Met Glu Ser Ala Glu Gln Lys Glu Gln Gly Leu Ser 2950 2955 2960	9117		
35	AGG GAT GTC ACA ACC GTG TGG AAG TTG CGT ATT GTA AGC TAT TCA AAA Arg Asp Val Thr Thr Val Trp Lys Leu Arg Ile Val Ser Tyr Ser Lys 2965 2970 2975	9165		
	AAA GAA AAA GAT TCA GTT ATA CTG AGT ATT TGG CGT CCA TCA TCA GAT Lys Glu Lys Asp Ser Val Ile Leu Ser Ile Trp Arg Pro Ser Ser Asp 2980 2985 2990 2995	9213		
40	TTA TAT TCT CTG TTA ACA GAA GGA AAG AGA TAC AGA ATT TAT CAT CTT Leu Tyr Ser Leu Leu Thr Glu Gly Lys Arg Tyr Arg Ile Tyr His Leu 3000 3005 3010	9261		
45	GCA ACT TCA AAA TCT AAA AGT AAA TCT GAA AGA GCT AAC ATA CAG TTA Ala Thr Ser Lys Ser Lys Ser Lys Ser Glu Arg Ala Asn Ile Gln Leu 3015 3020 3025	9309		
50	GCA GCG ACA AAA AAA ACT CAG TAT CAA CAA CTA CCG GTT TCA GAT GAA Ala Ala Thr Lys Lys Thr Gln Tyr Gln Gln Leu Pro Val Ser Asp Glu 3030 3035 3040	9357		
55	ATT TTA TTT CAG ATT TAC CAG CCA CGG GAG CCC CTT CAC TTC AGC AAA Ile Leu Phe Gln Ile Tyr Gln Pro Arg Glu Pro Leu His Phe Ser Lys 3045 3050 3055	9405		
	TTT TTA GAT CCA GAC TTT CAG CCA TCT TGT TCT GAG GTG GAC CTA ATA Phe Leu Asp Pro Asp Phe Gln Pro Ser Cys Ser Glu Val Asp Leu Ile 3060 3065 3070 3075	9453		
60	GGA TTT GTC GTT TCT GTT GTG AAA AAA ACA GGA CTT GCC CCT TTC GTC Gly Phe Val Val Ser Val Val Lys Lys Thr Gly Leu Ala Pro Phe Val 3080 3085 3090	9501		



5	TAT TTG TCA GAC GAA TGT TAC AAT TTA CTG GCA ATA AAG TTT TGG ATA Tyr Leu Ser Asp Glu Cys Tyr Asn Leu Leu Ala Ile Lys Phe Trp Ile 3095 3100 3105	9549
10	GAC CTT AAT GAG GAC ATT ATT AAG CCT CAT ATG TTA ATT GCT GCA AGC Asp Leu Asn Glu Asp Ile Ile Lys Pro His Met Leu Ile Ala Ala Ser 3110 3115 3120	9597
15	AAC CTC CAG TGG CGA CCA GAA TCC AAA TCA GGC CTT CTT ACT TTA TTT Asn Leu Gln Trp Arg Pro Glu Ser Lys Ser Gly Leu Leu Thr Leu Phe 3125 3130 3135	9645
20	GCT GGA GAT TTT TCT GTG TTT TCT GCT AGT CCA AAA GAG GGC CAC TTT Ala Gly Asp Phe Ser Val Phe Ser Ala Ser Pro Lys Glu Gly His Phe 3140 3145 3150 3155	9693
25	CAA GAG ACA TTC AAC AAA ATG AAA AAT ACT GTT GAG AAT ATT GAC ATA Gln Glu Thr Phe Asn Lys Met Lys Asn Thr Val Glu Asn Ile Asp Ile 3160 3165 3170	9741
30	CTT TGC AAT GAA GCA GAA AAC AAG CTT ATG CAT ATA CTG CAT GCA AAT Leu Cys Asn Glu Ala Glu Asn Lys Leu Met His Ile Leu His Ala Asn 3175 3180 3185	9789
35	GAT CCC AAG TGG TCC ACC CCA ACT AAA GAC TGT ACT TCA GGG CCG TAC Asp Pro Lys Trp Ser Thr Pro Thr Lys Asp Cys Thr Ser Gly Pro Tyr 3190 3195 3200	9837
40	ACT GCT CAA ATC ATT CCT GGT ACA GGA AAC AAG CTT CTG ATG TCT TCT Thr Ala Gln Ile Ile Pro Gly Thr Gly Asn Lys Leu Leu Met Ser Ser 3205 3210 3215	9885
45	CCT AAT TGT GAG ATA TAT TAT CAA AGT CCT TTA TCA CTT TGT ATG GCC Pro Asn Cys Glu Ile Tyr Tyr Gln Ser Pro Leu Ser Leu Cys Met Ala 3220 3225 3230 3235	9933
50	AAA AGG AAG TCT GTT TCC ACA CCT GTC TCA GCC CAG ATG ACT TCA AAG Lys Arg Lys Ser Val Ser Thr Pro Val Ser Ala Gln Met Thr Ser Lys 3240 3245 3250	9981
55	TCT TGT AAA GGG GAG AAA GAG ATT GAT GAC CAA AAG AAC TGC AAA AAG Ser Cys Lys Gly Glu Lys Glu Ile Asp Asp Gln Lys Asn Cys Lys Lys 3255 3260 3265	10029
60	AGA AGA GCC TTG GAT TTC TTG AGT AGA CTG CCT TTA CCT CCA CCT GTT Arg Arg Ala Leu Asp Phe Leu Ser Arg Leu Pro Leu Pro Pro Pro Val 3270 3275 3280	10077
65	AGT CCC ATT TGT ACA TTT GTT TCT CCG GCT GCA CAG AAG GCA TTT CAG Ser Pro Ile Cys Thr Phe Val Ser Pro Ala Ala Gln Lys Ala Phe Gln 3285 3290 3295	10125
70	CCA CCA AGG AGT TGT GGC ACC AAA TAC GAA ACA CCC ATA AAG AAA AAA Pro Pro Arg Ser Cys Gly Thr Lys Tyr Glu Thr Pro Ile Lys Lys Lys 3300 3305 3310 3315	10173
75	GAA CTG AAT TCT CCT CAG ATG ACT CCA TTT AAA AAA TTC AAT GAA ATT Glu Leu Asn Ser Pro Gln Met Thr Pro Phe Lys Lys Phe Asn Glu Ile 3320 3325 3330	10221

TCT CTT TTG GAA AGT AAT TCA ATA GCT GAC GAA GAA CTT GCA TTG ATA 10269  
 Ser Leu Leu Glu Ser Asn Ser Ile Ala Asp Glu Glu Leu Ala Leu Ile  
 3335 3340 3345  
 5 AAT ACC CAA GCT CTT TTG TCT GGT TCA ACA GGA GAA AAA CAA TTT ATA 10317  
 Asn Thr Gln Ala Leu Leu Ser Gly Ser Thr Gly Glu Lys Gln Phe Ile  
 3350 3355 3360  
 10 TCT GTC AGT GAA TCC ACT AGG ACT GCT CCC ACC AGT TCA GAA GAT TAT 10365  
 Ser Val Ser Glu Ser Thr Arg Thr Ala Pro Thr Ser Ser Glu Asp Tyr  
 3365 3370 3375  
 CTC AGA CTG AAA CGA CGT TGT ACT ACA TCT CTG ATC AAA GAA CAG GAG 10413  
 15 Leu Arg Leu Lys Arg Arg Cys Thr Thr Ser Leu Ile Lys Glu Gln Glu  
 3380 3385 3390 3395  
 AGT TCC CAG GCC AGT ACG GAA GAA TGT GAG AAA AAT AAG CAG GAC ACA 10461  
 20 Ser Ser Gln Ala Ser Thr Glu Glu Cys Glu Lys Asn Lys Gln Asp Thr  
 3400 3405 3410  
 ATT ACA ACT AAA AAA TAT ATC TAA 10485  
 Ile Thr Thr Lys Lys Tyr Ile  
 3415  
 25

## (2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:  
 30 (A) LENGTH: 3418 amino acids  
 (B) TYPE: amino acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

35 (ii) MOLECULE TYPE: protein  
 (v) FRAGMENT TYPE: internal

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

40 Met Pro Ile Gly Ser Lys Glu Arg Pro Thr Phe Phe Glu Ile Phe Lys  
 1 5 10 15  
 Thr Arg Cys Asn Lys Ala Asp Leu Gly Pro Ile Ser Leu Asn Trp Phe  
 20 25 30  
 Glu Glu Leu Ser Ser Glu Ala Pro Pro Tyr Asn Ser Glu Pro Ala Glu  
 35 40 45  
 45 Glu Ser Glu His Lys Asn Asn Asn Tyr Glu Pro Asn Leu Phe Lys Thr  
 50 55 60  
 Pro Gln Arg Lys Ser Ser Tyr Asn Glu Leu Ala Ser Thr Pro Ile Ile  
 65 70 75 80  
 50 Phe Lys Glu Gln Gly Leu Thr Leu Pro Leu Tyr Gln Ser Pro Val Lys  
 85 90 95  
 Glu Leu Asp Lys Phe Lys Leu Asp Leu Gly Arg Asn Val Pro Asn Ser  
 100 105 110  
 Arg His Lys Ser Leu Arg Thr Val Lys Thr Lys Met Asp Gln Ala Asp  
 115 120 125  
 55 Asp Val Ser Cys Pro Leu Leu Asn Ser Cys Leu Ser Glu Ser Pro Val  
 130 135 140  
 Val Leu Gln Cys Thr His Val Thr Pro Gln Arg Asp Lys Ser Val Val  
 145 150 155 160  
 60 Cys Gly Ser Leu Phe His Thr Pro Lys Phe Val Lys Gly Arg Gln Thr  
 165 170 175  
 Pro Lys His Ile Ser Glu Ser Leu Gly Ala Glu Val Asp Pro Asp Met

				180				185				190				
	Ser	Trp	Ser	Ser	Ser	Leu	Ala	Thr	Pro	Pro	Thr	Leu	Ser	Ser	Thr	Val
			195					200				205				
5	Leu	Ile	Val	Arg	Asn	Glu	Glu	Ala	Ser	Glu	Thr	Val	Phe	Pro	His	Asp
		210					215					220				
	Thr	Thr	Ala	Asn	Val	Lys	Ser	Tyr	Phe	Ser	Asn	His	Asp	Glu	Ser	Leu
	225				230						235				240	
	Lys	Lys	Asn	Asp	Arg	Phe	Ile	Ala	Ser	Val	Thr	Asp	Ser	Glu	Asn	Thr
10				245						250					255	
	Asn	Gln	Arg	Glu	Ala	Ala	Ser	His	Gly	Phe	Gly	Lys	Thr	Ser	Gly	Asn
			260						265					270		
	Ser	Phe	Lys	Val	Asn	Ser	Cys	Lys	Asp	His	Ile	Gly	Lys	Ser	Met	Pro
			275					280					285			
15	Asn	Val	Leu	Glu	Asp	Glu	Val	Tyr	Glu	Thr	Val	Val	Asp	Thr	Ser	Glu
		290					295					300				
	Glu	Asp	Ser	Phe	Ser	Leu	Cys	Phe	Ser	Lys	Cys	Arg	Thr	Lys	Asn	Leu
	305					310					315				320	
	Gln	Lys	Val	Arg	Thr	Ser	Lys	Thr	Arg	Lys	Lys	Ile	Phe	His	Glu	Ala
20				325						330					335	
	Asn	Ala	Asp	Glu	Cys	Glu	Lys	Ser	Lys	Asn	Gln	Val	Lys	Glu	Lys	Tyr
			340						345					350		
	Ser	Phe	Val	Ser	Glu	Val	Glu	Pro	Asn	Asp	Thr	Asp	Pro	Leu	Asp	Ser
			355					360					365			
25	Asn	Val	Ala	His	Gln	Lys	Pro	Phe	Glu	Ser	Gly	Ser	Asp	Lys	Ile	Ser
		370					375					380				
	Lys	Glu	Val	Val	Pro	Ser	Leu	Ala	Cys	Glu	Trp	Ser	Gln	Leu	Thr	Leu
	385					390					395				400	
	Ser	Gly	Leu	Asn	Gly	Ala	Gln	Met	Glu	Lys	Ile	Pro	Leu	Leu	His	Ile
30				405						410					415	
	Ser	Ser	Cys	Asp	Gln	Asn	Ile	Ser	Glu	Lys	Asp	Leu	Leu	Asp	Thr	Glu
			420						425					430		
	Asn	Lys	Arg	Lys	Lys	Asp	Phe	Leu	Thr	Ser	Glu	Asn	Ser	Leu	Pro	Arg
			435					440					445			
35	Ile	Ser	Ser	Leu	Pro	Lys	Ser	Glu	Lys	Pro	Leu	Asn	Glu	Glu	Thr	Val
		450					455					460				
	Val	Asn	Lys	Arg	Asp	Glu	Glu	Gln	His	Leu	Glu	Ser	His	Thr	Asp	Cys
	465					470					475				480	
	Ile	Leu	Ala	Val	Lys	Gln	Ala	Ile	Ser	Gly	Thr	Ser	Pro	Val	Ala	Ser
40				485						490					495	
	Ser	Phe	Gln	Gly	Ile	Lys	Lys	Ser	Ile	Phe	Arg	Ile	Arg	Glu	Ser	Pro
			500						505					510		
	Lys	Glu	Thr	Phe	Asn	Ala	Ser	Phe	Ser	Gly	His	Met	Thr	Asp	Pro	Asn
			515					520					525			
45	Phe	Lys	Lys	Glu	Thr	Glu	Ala	Ser	Glu	Ser	Gly	Leu	Glu	Ile	His	Thr
		530					535					540				
	Val	Cys	Ser	Gln	Lys	Glu	Asp	Ser	Leu	Cys	Pro	Asn	Leu	Ile	Asp	Asn
	545					550					555				560	
	Gly	Ser	Trp	Pro	Ala	Thr	Thr	Thr	Gln	Asn	Ser	Val	Ala	Leu	Lys	Asn
50				565						570					575	
	Ala	Gly	Leu	Ile	Ser	Thr	Leu	Lys	Lys	Lys	Thr	Asn	Lys	Phe	Ile	Tyr
			580						585					590		
	Ala	Ile	His	Asp	Glu	Thr	Ser	Tyr	Lys	Gly	Lys	Lys	Ile	Pro	Lys	Asp
			595					600					605			
55	Gln	Lys	Ser	Glu	Leu	Ile	Asn	Cys	Ser	Ala	Gln	Phe	Glu	Ala	Asn	Ala
		610					615					620				
	Phe	Glu	Ala	Pro	Leu	Thr	Phe	Ala	Asn	Ala	Asp	Ser	Gly	Leu	Leu	His
	625					630					635				640	
	Ser	Ser	Val	Lys	Arg	Ser	Cys	Ser	Gln	Asn	Asp	Ser	Glu	Glu	Pro	Thr
60				645						650					655	
	Leu	Ser	Leu	Thr	Ser	Ser	Phe	Gly	Thr	Ile	Leu	Arg	Lys	Cys	Ser	Arg
			660						665					670		

	Asn	Glu	Thr	Cys	Ser	Asn	Asn	Thr	Val	Ile	Ser	Gln	Asp	Leu	Asp	Tyr
			675					680					685			
5	Lys	Glu	Ala	Lys	Cys	Asn	Lys	Glu	Lys	Leu	Gln	Leu	Phe	Ile	Thr	Pro
		690				695					700					
	Glu	Ala	Asp	Ser	Leu	Ser	Cys	Leu	Gln	Glu	Gly	Gln	Cys	Glu	Asn	Asp
		705				710					715				720	
	Pro	Lys	Ser	Lys	Lys	Val	Ser	Asp	Ile	Lys	Glu	Glu	Val	Leu	Ala	Ala
					725					730					735	
10	Ala	Cys	His	Pro	Val	Gln	His	Ser	Lys	Val	Glu	Tyr	Ser	Asp	Thr	Asp
				740					745					750		
	Phe	Gln	Ser	Gln	Lys	Ser	Leu	Leu	Tyr	Asp	His	Glu	Asn	Ala	Ser	Thr
		755						760					765			
	Leu	Ile	Leu	Thr	Pro	Thr	Ser	Lys	Asp	Val	Leu	Ser	Asn	Leu	Val	Met
15		770					775					780				
	Ile	Ser	Arg	Gly	Lys	Glu	Ser	Tyr	Lys	Met	Ser	Asp	Lys	Leu	Lys	Gly
		785				790					795					800
	Asn	Asn	Tyr	Glu	Ser	Asp	Val	Glu	Leu	Thr	Lys	Asn	Ile	Pro	Met	Glu
					805				810						815	
20	Lys	Asn	Gln	Asp	Val	Cys	Ala	Leu	Asn	Glu	Asn	Tyr	Lys	Asn	Val	Glu
				820					825					830		
	Leu	Leu	Pro	Pro	Glu	Lys	Tyr	Met	Arg	Val	Ala	Ser	Pro	Ser	Arg	Lys
			835					840					845			
	Val	Gln	Phe	Asn	Gln	Asn	Thr	Asn	Leu	Arg	Val	Ile	Gln	Lys	Asn	Gln
25		850					855					860				
	Glu	Glu	Thr	Thr	Ser	Ile	Ser	Lys	Ile	Thr	Val	Asn	Pro	Asp	Ser	Glu
		865				870					875					880
	Glu	Leu	Phe	Ser	Asp	Asn	Glu	Asn	Asn	Phe	Val	Phe	Gln	Val	Ala	Asn
					885					890						895
30	Glu	Arg	Asn	Asn	Leu	Ala	Leu	Gly	Asn	Thr	Lys	Glu	Leu	His	Glu	Thr
			900					905						910		
	Asp	Leu	Thr	Cys	Val	Asn	Glu	Pro	Ile	Phe	Lys	Asn	Ser	Thr	Met	Val
			915					920					925			
	Leu	Tyr	Gly	Asp	Thr	Gly	Asp	Lys	Gln	Ala	Thr	Gln	Val	Ser	Ile	Lys
35		930					935					940				
	Lys	Asp	Leu	Val	Tyr	Val	Leu	Ala	Glu	Glu	Asn	Lys	Asn	Ser	Val	Lys
		945				950					955					960
	Gln	His	Ile	Lys	Met	Thr	Leu	Gly	Gln	Asp	Leu	Lys	Ser	Asp	Ile	Ser
					965					970					975	
40	Leu	Asn	Ile	Asp	Lys	Ile	Pro	Glu	Lys	Asn	Asn	Asp	Tyr	Met	Asn	Lys
			980					985						990		
	Trp	Ala	Gly	Leu	Leu	Gly	Pro	Ile	Ser	Asn	His	Ser	Phe	Gly	Gly	Ser
		995					1000						1005			
	Phe	Arg	Thr	Ala	Ser	Asn	Lys	Glu	Ile	Lys	Leu	Ser	Glu	His	Asn	Ile
45		1010					1015					1020				
	Lys	Lys	Ser	Lys	Met	Phe	Phe	Lys	Asp	Ile	Glu	Glu	Gln	Tyr	Pro	Thr
		1025				1030					1035					104
	Ser	Leu	Ala	Cys	Val	Glu	Ile	Val	Asn	Thr	Leu	Ala	Leu	Asp	Asn	Gln
					1045					1050					1055	
50	Lys	Lys	Leu	Ser	Lys	Pro	Gln	Ser	Ile	Asn	Thr	Val	Ser	Ala	His	Leu
				1060					1065					1070		
	Gln	Ser	Ser	Val	Val	Val	Ser	Asp	Cys	Lys	Asn	Ser	His	Ile	Thr	Pro
		1075						1080					1085			
	Gln	Met	Leu	Phe	Ser	Lys	Gln	Asp	Phe	Asn	Ser	Asn	His	Asn	Leu	Thr
55		1090					1095					1100				
	Pro	Ser	Gln	Lys	Ala	Glu	Ile	Thr	Glu	Leu	Ser	Thr	Ile	Leu	Glu	Glu
		1105				1110					1115					112
	Ser	Gly	Ser	Gln	Phe	Glu	Phe	Thr	Gln	Phe	Arg	Lys	Pro	Ser	Tyr	Ile
					1125					1130					1135	
60	Leu	Gln	Lys	Ser	Thr	Phe	Glu	Val	Pro	Glu	Asn	Gln	Met	Thr	Ile	Leu
				1140					1145					1150		
	Lys	Thr	Thr	Ser	Glu	Glu	Cys	Arg	Asp	Ala	Asp	Leu	His	Val	Ile	Met

	1155	1160	1165
	Asn Ala Pro Ser Ile Gly Gln Val Asp Ser Ser Lys Gln Phe Glu Gly		
	1170	1175	1180
5	Thr Val Glu Ile Lys Arg Lys Phe Ala Gly Leu Leu Lys Asn Asp Cys		
	1185	1190	1195
	Asn Lys Ser Ala Ser Gly Tyr Leu Thr Asp Glu Asn Glu Val Gly Phe		
	1205	1210	1215
10	Arg Gly Phe Tyr Ser Ala His Gly Thr Lys Leu Asn Val Ser Thr Glu		
	1220	1225	1230
	Ala Leu Gln Lys Ala Val Lys Leu Phe Ser Asp Ile Glu Asn Ile Ser		
	1235	1240	1245
	Glu Glu Thr Ser Ala Glu Val His Pro Ile Ser Leu Ser Ser Ser Lys		
	1250	1255	1260
15	Cys His Asp Ser Val Val Ser Met Phe Lys Ile Glu Asn His Asn Asp		
	1265	1270	1275
	Lys Thr Val Ser Glu Lys Asn Asn Lys Cys Gln Leu Ile Leu Gln Asn		
	1285	1290	1295
20	Asn Ile Glu Met Thr Thr Gly Thr Phe Val Glu Glu Ile Thr Glu Asn		
	1300	1305	1310
	Tyr Lys Arg Asn Thr Glu Asn Glu Asp Asn Lys Tyr Thr Ala Ala Ser		
	1315	1320	1325
	Arg Asn Ser His Asn Leu Glu Phe Asp Gly Ser Asp Ser Ser Lys Asn		
	1330	1335	1340
25	Asp Thr Val Cys Ile His Lys Asp Glu Thr Asp Leu Leu Phe Thr Asp		
	1345	1350	1355
	Gln His Asn Ile Cys Leu Lys Leu Ser Gly Gln Phe Met Lys Glu Gly		
	1365	1370	1375
30	Asn Thr Gln Ile Lys Glu Asp Leu Ser Asp Leu Thr Phe Leu Glu Val		
	1380	1385	1390
	Ala Lys Ala Gln Glu Ala Cys His Gly Asn Thr Ser Asn Lys Glu Gln		
	1395	1400	1405
	Leu Thr Ala Thr Lys Thr Glu Gln Asn Ile Lys Asp Phe Glu Thr Ser		
	1410	1415	1420
35	Asp Thr Phe Phe Gln Thr Ala Ser Gly Lys Asn Ile Ser Val Ala Lys		
	1425	1430	1435
	Glu Ser Phe Asn Lys Ile Val Asn Phe Phe Asp Gln Lys Pro Glu Glu		
	1445	1450	1455
40	Leu His Asn Phe Ser Leu Asn Ser Glu Leu His Ser Asp Ile Arg Lys		
	1460	1465	1470
	Asn Lys Met Asp Ile Leu Ser Tyr Glu Glu Thr Asp Ile Val Lys His		
	1475	1480	1485
	Lys Ile Leu Lys Glu Ser Val Pro Val Gly Thr Gly Asn Gln Leu Val		
	1490	1495	1500
45	Thr Phe Gln Gly Gln Pro Glu Arg Asp Glu Lys Ile Lys Glu Pro Thr		
	1505	1510	1515
	Leu Leu Gly Phe His Thr Ala Ser Gly Lys Lys Val Lys Ile Ala Lys		
	1525	1530	1535
50	Glu Ser Leu Asp Lys Val Lys Asn Leu Phe Asp Glu Lys Glu Gln Gly		
	1540	1545	1550
	Thr Ser Glu Ile Thr Ser Phe Ser His Gln Trp Ala Lys Thr Leu Lys		
	1555	1560	1565
	Tyr Arg Glu Ala Cys Lys Asp Leu Glu Leu Ala Cys Glu Thr Ile Glu		
	1570	1575	1580
55	Ile Thr Ala Ala Pro Lys Cys Lys Glu Met Gln Asn Ser Leu Asn Asn		
	1585	1590	1595
	Asp Lys Asn Leu Val Ser Ile Glu Thr Val Val Pro Pro Lys Leu Leu		
	1605	1610	1615
60	Ser Asp Asn Leu Cys Arg Gln Thr Glu Asn Leu Lys Thr Ser Lys Ser		
	1620	1625	1630
	Ile Phe Leu Lys Val Lys Val His Glu Asn Val Glu Lys Glu Thr Ala		
	1635	1640	1645

Lys Ser Pro Ala Thr Cys Tyr Thr Asn Gln Ser Pro Tyr Ser Val Ile  
 1650 1655 1660  
 5 Glu Asn Ser Ala Leu Ala Phe Tyr Thr Ser Cys Ser Arg Lys Thr Ser  
 1665 1670 1675 168  
 Val Ser Gln Thr Ser Leu Leu Glu Ala Lys Lys Trp Leu Arg Glu Gly  
 1685 1690 1695  
 Ile Phe Asp Gly Gln Pro Glu Arg Ile Asn Thr Ala Asp Tyr Val Gly  
 1700 1705 1710  
 10 Asn Tyr Leu Tyr Glu Asn Asn Ser Asn Ser Thr Ile Ala Glu Asn Asp  
 1715 1720 1725  
 Lys Asn His Leu Ser Glu Lys Gln Asp Thr Tyr Leu Ser Asn Ser Ser  
 1730 1735 1740  
 15 Met Ser Asn Ser Tyr Ser Tyr His Ser Asp Glu Val Tyr Asn Asp Ser  
 1745 1750 1755 176  
 Gly Tyr Leu Ser Lys Asn Lys Leu Asp Ser Gly Ile Glu Pro Val Leu  
 1765 1770 1775  
 Lys Asn Glu Asp Gln Lys Asn Thr Ser Phe Ser Lys Val Ile Ser  
 1780 1785 1790  
 20 Asn Val Lys Asp Ala Asn Ala Tyr Pro Gln Thr Val Asn Glu Asp Ile  
 1795 1800 1805  
 Cys Val Glu Glu Leu Val Thr Ser Ser Ser Pro Cys Lys Asn Lys Asn  
 1810 1815 1820  
 25 Ala Ala Ile Lys Leu Ser Ile Ser Asn Ser Asn Asn Phe Glu Val Gly  
 1825 1830 1835 184  
 Pro Pro Ala Phe Arg Ile Ala Ser Gly Lys Ile Val Cys Val Ser His  
 1845 1850 1855  
 Glu Thr Ile Lys Lys Val Lys Asp Ile Phe Thr Asp Ser Phe Ser Lys  
 1860 1865 1870  
 30 Val Ile Lys Glu Asn Asn Glu Asn Lys Ser Lys Ile Cys Gln Thr Lys  
 1875 1880 1885  
 Ile Met Ala Gly Cys Tyr Glu Ala Leu Asp Asp Ser Glu Asp Ile Leu  
 1890 1895 1900  
 35 His Asn Ser Leu Asp Asn Asp Glu Cys Ser Thr His Ser His Lys Val  
 1905 1910 1915 192  
 Phe Ala Asp Ile Gln Ser Glu Glu Ile Leu Gln His Asn Gln Asn Met  
 1925 1930 1935  
 Ser Gly Leu Glu Lys Val Ser Lys Ile Ser Pro Cys Asp Val Ser Leu  
 1940 1945 1950  
 40 Glu Thr Ser Asp Ile Cys Lys Cys Ser Ile Gly Lys Leu His Lys Ser  
 1955 1960 1965  
 Val Ser Ser Ala Asn Thr Cys Gly Ile Phe Ser Thr Ala Ser Gly Lys  
 1970 1975 1980  
 45 Ser Val Gln Val Ser Asp Ala Ser Leu Gln Asn Ala Arg Gln Val Phe  
 1985 1990 1995 200  
 Ser Glu Ile Glu Asp Ser Thr Lys Gln Val Phe Ser Lys Val Leu Phe  
 2005 2010 2015  
 Lys Ser Asn Glu His Ser Asp Gln Leu Thr Arg Glu Glu Asn Thr Ala  
 2020 2025 2030  
 50 Ile Arg Thr Pro Glu His Leu Ile Ser Gln Lys Gly Phe Ser Tyr Asn  
 2035 2040 2045  
 Val Val Asn Ser Ser Ala Phe Ser Gly Phe Ser Thr Ala Ser Gly Lys  
 2050 2055 2060  
 55 Gln Val Ser Ile Leu Glu Ser Ser Leu His Lys Val Lys Gly Val Leu  
 2065 2070 2075 208  
 Glu Glu Phe Asp Leu Ile Arg Thr Glu His Ser Leu His Tyr Ser Pro  
 2085 2090 2095  
 Thr Ser Arg Gln Asn Val Ser Lys Ile Leu Pro Arg Val Asp Lys Arg  
 2100 2105 2110  
 60 Asn Pro Glu His Cys Val Asn Ser Glu Met Glu Lys Thr Cys Ser Lys  
 2115 2120 2125  
 Glu Phe Lys Leu Ser Asn Asn Leu Asn Val Glu Gly Gly Ser Ser Glu

	2130	2135	2140
	Asn Asn His Ser Ile Lys Val Ser Pro Tyr Leu Ser Gln Phe Gln Gln		
	2145	2150	2155
5	Asp Lys Gln Gln Leu Val Leu Gly Thr Lys Val Ser Leu Val Glu Asn		
	2165	2170	2175
	Ile His Val Leu Gly Lys Glu Gln Ala Ser Pro Lys Asn Val Lys Met		
	2180	2185	2190
10	Glu Ile Gly Lys Thr Glu Thr Phe Ser Asp Val Pro Val Lys Thr Asn		
	2195	2200	2205
	Ile Glu Val Cys Ser Thr Tyr Ser Lys Asp Ser Glu Asn Tyr Phe Glu		
	2210	2215	2220
	Thr Glu Ala Val Glu Ile Ala Lys Ala Phe Met Glu Asp Asp Glu Leu		
	2225	2230	2235
15	Thr Asp Ser Lys Leu Pro Ser His Ala Thr His Ser Leu Phe Thr Cys		
	2245	2250	2255
	Pro Glu Asn Glu Glu Met Val Leu Ser Asn Ser Arg Ile Gly Lys Arg		
	2260	2265	2270
20	Arg Gly Glu Pro Leu Ile Leu Val Gly Glu Pro Ser Ile Lys Arg Asn		
	2275	2280	2285
	Leu Leu Asn Glu Phe Asp Arg Ile Ile Glu Asn Gln Glu Lys Ser Leu		
	2290	2295	2300
	Lys Ala Ser Lys Ser Thr Pro Asp Gly Thr Ile Lys Asp Arg Arg Leu		
	2305	2310	2315
25	Phe Met His His Val Ser Leu Glu Pro Ile Thr Cys Val Pro Phe Arg		
	2325	2330	2335
	Thr Thr Lys Glu Arg Gln Glu Ile Gln Asn Pro Asn Phe Thr Ala Pro		
	2340	2345	2350
30	Gly Gln Glu Phe Leu Ser Lys Ser His Leu Tyr Glu His Leu Thr Leu		
	2355	2360	2365
	Glu Lys Ser Ser Ser Asn Leu Ala Val Ser Gly His Pro Phe Tyr Gln		
	2370	2375	2380
	Val Ser Ala Thr Arg Asn Glu Lys Met Arg His Leu Ile Thr Thr Gly		
	2385	2390	2395
35	Arg Pro Thr Lys Val Phe Val Pro Pro Phe Lys Thr Lys Ser His Phe		
	2405	2410	2415
	His Arg Val Glu Gln Cys Val Arg Asn Ile Asn Leu Glu Glu Asn Arg		
	2420	2425	2430
40	Gln Lys Gln Asn Ile Asp Gly His Gly Ser Asp Asp Ser Lys Asn Lys		
	2435	2440	2445
	Ile Asn Asp Asn Glu Ile His Gln Phe Asn Lys Asn Asn Ser Asn Gln		
	2450	2455	2460
	Ala Ala Ala Val Thr Phe Thr Lys Cys Glu Glu Glu Pro Leu Asp Leu		
	2465	2470	2475
45	Ile Thr Ser Leu Gln Asn Ala Arg Asp Ile Gln Asp Met Arg Ile Lys		
	2485	2490	2495
	Lys Lys Gln Arg Gln Arg Val Phe Pro Gln Pro Gly Ser Leu Tyr Leu		
	2500	2505	2510
50	Ala Lys Thr Ser Thr Leu Pro Arg Ile Ser Leu Lys Ala Ala Val Gly		
	2515	2520	2525
	Gly Gln Val Pro Ser Ala Cys Ser His Lys Gln Leu Tyr Thr Tyr Gly		
	2530	2535	2540
	Val Ser Lys His Cys Ile Lys Ile Asn Ser Lys Asn Ala Glu Ser Phe		
	2545	2550	2555
55	Gln Phe His Thr Glu Asp Tyr Phe Gly Lys Glu Ser Leu Trp Thr Gly		
	2565	2570	2575
	Lys Gly Ile Gln Leu Ala Asp Gly Gly Trp Leu Ile Pro Ser Asn Asp		
	2580	2585	2590
60	Gly Lys Ala Gly Lys Glu Glu Phe Tyr Arg Ala Leu Cys Asp Thr Pro		
	2595	2600	2605
	Gly Val Asp Pro Lys Leu Ile Ser Arg Ile Trp Val Tyr Asn His Tyr		
	2610	2615	2620

Arg Trp Ile Ile Trp Lys Leu Ala Ala Met Glu Cys Ala Phe Pro Lys  
 2625 2630 2635 264  
 Glu Phe Ala Asn Arg Cys Leu Ser Pro Glu Arg Val Leu Leu Gln Leu  
 2645 2650 2655  
 5 Lys Tyr Arg Tyr Asp Thr Glu Ile Asp Arg Ser Arg Arg Ser Ala Ile  
 2660 2665 2670  
 Lys Lys Ile Met Glu Arg Asp Asp Thr Ala Ala Lys Thr Leu Val Leu  
 2675 2680 2685  
 10 Cys Val Ser Asp Ile Ile Ser Leu Ser Ala Asn Ile Ser Glu Thr Ser  
 2690 2695 2700  
 Ser Asn Lys Thr Ser Ser Ala Asp Thr Gln Lys Val Ala Ile Ile Glu  
 2705 2710 2715 272  
 Leu Thr Asp Gly Trp Tyr Ala Val Lys Ala Gln Leu Asp Pro Pro Leu  
 2725 2730 2735  
 15 Leu Ala Val Leu Lys Asn Gly Arg Leu Thr Val Gly Gln Lys Ile Ile  
 2740 2745 2750  
 Leu His Gly Ala Glu Leu Val Gly Ser Pro Asp Ala Cys Thr Pro Leu  
 2755 2760 2765  
 20 Glu Ala Pro Glu Ser Leu Met Leu Lys Ile Ser Ala Asn Ser Thr Arg  
 2770 2775 2780  
 Pro Ala Arg Trp Tyr Thr Lys Leu Gly Phe Phe Pro Asp Pro Arg Pro  
 2785 2790 2795 280  
 Phe Pro Leu Pro Leu Ser Ser Leu Phe Ser Asp Gly Gly Asn Val Gly  
 2805 2810 2815  
 25 Cys Val Asp Val Ile Ile Gln Arg Ala Tyr Pro Ile Gln Trp Met Glu  
 2820 2825 2830  
 Lys Thr Ser Ser Gly Leu Tyr Ile Phe Arg Asn Glu Arg Glu Glu Glu  
 2835 2840 2845  
 30 Lys Glu Ala Ala Lys Tyr Val Glu Ala Gln Gln Lys Arg Leu Glu Ala  
 2850 2855 2860  
 Leu Phe Thr Lys Ile Gln Glu Glu Phe Glu Glu His Glu Glu Asn Thr  
 2865 2870 2875 288  
 Thr Lys Pro Tyr Leu Pro Ser Arg Ala Leu Thr Arg Gln Gln Val Arg  
 2885 2890 2895  
 35 Ala Leu Gln Asp Gly Ala Glu Leu Tyr Glu Ala Val Lys Asn Ala Ala  
 2900 2905 2910  
 Asp Pro Ala Tyr Leu Glu Gly Tyr Phe Ser Glu Glu Gln Leu Arg Ala  
 2915 2920 2925  
 40 Leu Asn Asn His Arg Gln Met Leu Asn Asp Lys Lys Gln Ala Gln Ile  
 2930 2935 2940  
 Gln Leu Glu Ile Arg Lys Ala Met Glu Ser Ala Glu Gln Lys Glu Gln  
 2945 2950 2955 296  
 Gly Leu Ser Arg Asp Val Thr Thr Val Trp Lys Leu Arg Ile Val Ser  
 2965 2970 2975  
 45 Tyr Ser Lys Lys Glu Lys Asp Ser Val Ile Leu Ser Ile Trp Arg Pro  
 2980 2985 2990  
 Ser Ser Asp Leu Tyr Ser Leu Leu Thr Glu Gly Lys Arg Tyr Arg Ile  
 2995 3000 3005  
 50 Tyr His Leu Ala Thr Ser Lys Ser Lys Ser Lys Ser Glu Arg Ala Asn  
 3010 3015 3020  
 Ile Gln Leu Ala Ala Thr Lys Lys Thr Gln Tyr Gln Gln Leu Pro Val  
 3025 3030 3035 304  
 Ser Asp Glu Ile Leu Phe Gln Ile Tyr Gln Pro Arg Glu Pro Leu His  
 3045 3050 3055  
 55 Phe Ser Lys Phe Leu Asp Pro Asp Phe Gln Pro Ser Cys Ser Glu Val  
 3060 3065 3070  
 Asp Leu Ile Gly Phe Val Val Ser Val Val Lys Lys Thr Gly Leu Ala  
 3075 3080 3085  
 60 Pro Phe Val Tyr Leu Ser Asp Glu Cys Tyr Asn Leu Leu Ala Ile Lys  
 3090 3095 3100  
 Phe Trp Ile Asp Leu Asn Glu Asp Ile Ile Lys Pro His Met Leu Ile



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3105          3110          3115          312
Ala Ala Ser Asn Leu Gln Trp Arg Pro Glu Ser Lys Ser Gly Leu Leu
          3125          3130          3135
5  Thr Leu Phe Ala Gly Asp Phe Ser Val Phe Ser Ala Ser Pro Lys Glu
          3140          3145          3150
Gly His Phe Gln Glu Thr Phe Asn Lys Met Lys Asn Thr Val Glu Asn
          3155          3160          3165
10 Ile Asp Ile Leu Cys Asn Glu Ala Glu Asn Lys Leu Met His Ile Leu
          3170          3175          3180
His Ala Asn Asp Pro Lys Trp Ser Thr Pro Thr Lys Asp Cys Thr Ser
3185          3190          3195          320
Gly Pro Tyr Thr Ala Gln Ile Ile Pro Gly Thr Gly Asn Lys Leu Leu
          3205          3210          3215
15 Met Ser Ser Pro Asn Cys Glu Ile Tyr Tyr Gln Ser Pro Leu Ser Leu
          3220          3225          3230
Cys Met Ala Lys Arg Lys Ser Val Ser Thr Pro Val Ser Ala Gln Met
          3235          3240          3245
20 Thr Ser Lys Ser Cys Lys Gly Glu Lys Glu Ile Asp Asp Gln Lys Asn
          3250          3255          3260
Cys Lys Lys Arg Arg Ala Leu Asp Phe Leu Ser Arg Leu Pro Leu Pro
3265          3270          3275          328
Pro Pro Val Ser Pro Ile Cys Thr Phe Val Ser Pro Ala Ala Gln Lys
          3285          3290          3295
25 Ala Phe Gln Pro Pro Arg Ser Cys Gly Thr Lys Tyr Glu Thr Pro Ile
          3300          3305          3310
Lys Lys Lys Glu Leu Asn Ser Pro Gln Met Thr Pro Phe Lys Lys Phe
          3315          3320          3325
Asn Glu Ile Ser Leu Leu Glu Ser Asn Ser Ile Ala Asp Glu Glu Leu
30          3330          3335          3340
Ala Leu Ile Asn Thr Gln Ala Leu Leu Ser Gly Ser Thr Gly Glu Lys
3345          3350          3355          336
Gln Phe Ile Ser Val Ser Glu Ser Thr Arg Thr Ala Pro Thr Ser Ser
          3365          3370          3375
35 Glu Asp Tyr Leu Arg Leu Lys Arg Arg Cys Thr Thr Ser Leu Ile Lys
          3380          3385          3390
Glu Gln Glu Ser Ser Gln Ala Ser Thr Glu Glu Cys Glu Lys Asn Lys
          3395          3400          3405
40 Gln Asp Thr Ile Thr Thr Lys Lys Tyr Ile
          3410          3415

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## (2) INFORMATION FOR SEQ ID NO:6:

- (i) SEQUENCE CHARACTERISTICS:
- 45 (A) LENGTH: 10485 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: double  
(D) TOPOLOGY: linear
- 50 (ii) MOLECULE TYPE: cDNA  
(ix) FEATURE:
- (A) NAME/KEY: Coding Sequence  
(B) LOCATION: 229...10482  
55 (D) OTHER INFORMATION: BRCA2 (OMI2)

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

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GGTGGCGCGA GCTTCTGAAA CTAGGCGGCA GAGGCGGAGC CGCTGTGGCA CTGCTGCGCC 60
TCTGCTGCGC CTCGGGTGTC TTTTGCGGCG GTGGGTGCGC GCCGGGAGAA GCGTGAGGGG 120
ACAGATTTGT GACCGGCGCG GTTTTGTGCA GCTTACTCCG GCCAAAAAAG AACTGCACCT 180
CTGGAGCGGA CTTATTTACC AAGCATTTGA GGAATATCGT AGGTAAAA ATG CCT ATT 237

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Met Pro Ile

1

5	GGA TCC AAA GAG AGG CCA ACA TTT TTT GAA ATT TTT AAG ACA CGC TGC	285
	Gly Ser Lys Glu Arg Pro Thr Phe Phe Glu Ile Phe Lys Thr Arg Cys	
	5 10 15	
10	AAC AAA GCA GAT TTA GGA CCA ATA AGT CTT AAT TGG TTT GAA GAA CTT	333
	Asn Lys Ala Asp Leu Gly Pro Ile Ser Leu Asn Trp Phe Glu Glu Leu	
	20 25 30 35	
15	TCT TCA GAA GCT CCA CCC TAT AAT TCT GAA CCT GCA GAA GAA TCT GAA	381
	Ser Ser Glu Ala Pro Pro Tyr Asn Ser Glu Pro Ala Glu Glu Ser Glu	
	40 45 50	
20	CAT AAA AAC AAC AAT TAC GAA CCA AAC CTA TTT AAA ACT CCA CAA AGG	429
	His Lys Asn Asn Asn Tyr Glu Pro Asn Leu Phe Lys Thr Pro Gln Arg	
	55 60 65	
25	AAA CCA TCT TAT AAT CAG CTG GCT TCA ACT CCA ATA ATA TTC AAA GAG	477
	Lys Pro Ser Tyr Asn Gln Leu Ala Ser Thr Pro Ile Ile Phe Lys Glu	
	70 75 80	
30	CAA GGG CTG ACT CTG CCG CTG TAC CAA TCT CCT GTA AAA GAA TTA GAT	525
	Gln Gly Leu Thr Leu Pro Leu Tyr Gln Ser Pro Val Lys Glu Leu Asp	
	85 90 95	
35	AAA TTC AAA TTA GAC TTA GGA AGG AAT GTT CCC AAT AGT AGA CAT AAA	573
	Lys Phe Lys Leu Asp Leu Gly Arg Asn Val Pro Asn Ser Arg His Lys	
	100 105 110 115	
40	AGT CTT CGC ACA GTG AAA ACT AAA ATG GAT CAA GCA GAT GAT GTT TCC	621
	Ser Leu Arg Thr Val Lys Thr Lys Met Asp Gln Ala Asp Asp Val Ser	
	120 125 130	
45	TGT CCA CTT CTA AAT TCT TGT CTT AGT GAA AGT CCT GTT GTT CTA CAA	669
	Cys Pro Leu Leu Asn Ser Cys Leu Ser Glu Ser Pro Val Val Leu Gln	
	135 140 145	
50	TGT ACA CAT GTA ACA CCA CAA AGA GAT AAG TCA GTG GTA TGT GGG AGT	717
	Cys Thr His Val Thr Pro Gln Arg Asp Lys Ser Val Val Cys Gly Ser	
	150 155 160	
55	TTG TTT CAT ACA CCA AAG TTT GTG AAG GGT CGT CAG ACA CCA AAA CAT	765
	Leu Phe His Thr Pro Lys Phe Val Lys Gly Arg Gln Thr Pro Lys His	
	165 170 175	
60	ATT TCT GAA AGT CTA GGA GCT GAG GTG GAT CCT GAT ATG TCT TGG TCA	813
	Ile Ser Glu Ser Leu Gly Ala Glu Val Asp Pro Asp Met Ser Trp Ser	
	180 185 190 195	
65	AGT TCT TTA GCT ACA CCA CCC ACC CTT AGT TCT ACT GTG CTC ATA GTC	861
	Ser Ser Leu Ala Thr Pro Pro Thr Leu Ser Ser Thr Val Leu Ile Val	
	200 205 210	
70	AGA AAT GAA GAA GCA TCT GAA ACT GTA TTT CCT CAT GAT ACT ACT GCT	909
	Arg Asn Glu Glu Ala Ser Glu Thr Val Phe Pro His Asp Thr Thr Ala	
	215 220 225	
75	AAT GTG AAA AGC TAT TTT TCC AAT CAT GAT GAA AGT CTG AAG AAA AAT	957
	Asn Val Lys Ser Tyr Phe Ser Asn His Asp Glu Ser Leu Lys Lys Asn	

	230	235	240	
5	GAT AGA TTT ATC GCT TCT GTG ACA GAC AGT GAA AAC ACA AAT CAA AGA Asp Arg Phe Ile Ala Ser Val Thr Asp Ser Glu Asn Thr Asn Gln Arg 245 250 255	1005		
10	GAA GCT GCA AGT CAT GGA TTT GGA AAA ACA TCA GGG AAT TCA TTT AAA Glu Ala Ala Ser His Gly Phe Gly Lys Thr Ser Gly Asn Ser Phe Lys 260 265 270 275	1053		
15	GTA AAT AGC TGC AAA GAC CAC ATT GGA AAG TCA ATG CCA AAT GTC CTA Val Asn Ser Cys Lys Asp His Ile Gly Lys Ser Met Pro Asn Val Leu 280 285 290	1101		
20	GAA GAT GAA GTA TAT GAA ACA GTT GTA GAT ACC TCT GAA GAA GAT AGT Glu Asp Glu Val Tyr Glu Thr Val Val Asp Thr Ser Glu Glu Asp Ser 295 300 305	1149		
25	TTT TCA TTA TGT TTT TCT AAA TGT AGA ACA AAA AAT CTA CAA AAA GTA Phe Ser Leu Cys Phe Ser Lys Cys Arg Thr Lys Asn Leu Gln Lys Val 310 315 320	1197		
30	AGA ACT AGC AAG ACT AGG AAA AAA ATT TTC CAT GAA GCA AAC GCT GAT Arg Thr Ser Lys Thr Arg Lys Lys Ile Phe His Glu Ala Asn Ala Asp 325 330 335	1245		
35	GAA TGT GAA AAA TCT AAA AAC CAA GTG AAA GAA AAA TAC TCA TTT GTA Glu Cys Glu Lys Ser Lys Asn Gln Val Lys Glu Lys Tyr Ser Phe Val 340 345 350 355	1293		
40	TCT GAA GTG GAA CCA AAT GAT ACT GAT CCA TTA GAT TCA AAT GTA GCA Ser Glu Val Glu Pro Asn Asp Thr Asp Pro Leu Asp Ser Asn Val Ala 360 365 370	1341		
45	CAT CAG AAG CCC TTT GAG AGT GGA AGT GAC AAA ATC TCC AAG GAA GTT His Gln Lys Pro Phe Glu Ser Gly Ser Asp Lys Ile Ser Lys Glu Val 375 380 385	1389		
50	GTA CCG TCT TTG GCC TGT GAA TGG TCT CAA CTA ACC CTT TCA GGT CTA Val Pro Ser Leu Ala Cys Glu Trp Ser Gln Leu Thr Leu Ser Gly Leu 390 395 400	1437		
55	AAT GGA GCC CAG ATG GAG AAA ATA CCC CTA TTG CAT ATT TCT TCA TGT Asn Gly Ala Gln Met Glu Lys Ile Pro Leu Leu His Ile Ser Ser Cys 405 410 415	1485		
60	GAC CAA AAT ATT TCA GAA AAA GAC CTA TTA GAC ACA GAG AAC AAA AGA Asp Gln Asn Ile Ser Glu Lys Asp Leu Leu Asp Thr Glu Asn Lys Arg 420 425 430 435	1533		
65	AAG AAA GAT TTT CTT ACT TCA GAG AAT TCT TTG CCA CGT ATT TCT AGC Lys Lys Asp Phe Leu Thr Ser Glu Asn Ser Leu Pro Arg Ile Ser Ser 440 445 450	1581		
70	CTA CCA AAA TCA GAG AAG CCA TTA AAT GAG GAA ACA GTG GTA AAT AAG Leu Pro Lys Ser Glu Lys Pro Leu Asn Glu Glu Thr Val Val Asn Lys 455 460 465	1629		
75	AGA GAT GAA GAG CAG CAT CTT GAA TCT CAT ACA GAC TGC ATT CTT GCA Arg Asp Glu Glu Gln His Leu Glu Ser His Thr Asp Cys Ile Leu Ala 470 475 480	1677		

5	GTA AAG CAG GCA ATA TCT GGA ACT TCT CCA GTG GCT TCT TCA TTT CAG Val Lys Gln Ala Ile Ser Gly Thr Ser Pro Val Ala Ser Ser Phe Gln 485 490 495	1725
10	GGT ATC AAA AAG TCT ATA TTC AGA ATA AGA GAA TCA CCT AAA GAG ACT Gly Ile Lys Lys Ser Ile Phe Arg Ile Arg Glu Ser Pro Lys Glu Thr 500 505 510 515	1773
15	TTC AAT GCA AGT TTT TCA GGT CAT ATG ACT GAT CCA AAC TTT AAA AAA Phe Asn Ala Ser Phe Ser Gly His Met Thr Asp Pro Asn Phe Lys Lys 520 525 530	1821
20	GAA ACT GAA GCC TCT GAA AGT GGA CTG GAA ATA CAT ACT GTT TGC TCA Glu Thr Glu Ala Ser Glu Ser Gly Leu Glu Ile His Thr Val Cys Ser 535 540 545	1869
25	CAG AAG GAG GAC TCC TTA TGT CCA AAT TTA ATT GAT AAT GGA AGC TGG Gln Lys Glu Asp Ser Leu Cys Pro Asn Leu Ile Asp Asn Gly Ser Trp 550 555 560	1917
30	CCA GCC ACC ACC ACA CAG AAT TCT GTA GCT TTG AAG AAT GCA GGT TTA Pro Ala Thr Thr Thr Gln Asn Ser Val Ala Leu Lys Asn Ala Gly Leu 565 570 575	1965
35	ATA TCC ACT TTG AAA AAG AAA ACA AAT AAG TTT ATT TAT GCT ATA CAT Ile Ser Thr Leu Lys Lys Lys Thr Asn Lys Phe Ile Tyr Ala Ile His 580 585 590 595	2013
40	GAT GAA ACA TCT TAT AAA GGA AAA AAA ATA CCG AAA GAC CAA AAA TCA Asp Glu Thr Ser Tyr Lys Gly Lys Lys Ile Pro Lys Asp Gln Lys Ser 600 605 610	2061
45	GAA CTA ATT AAC TGT TCA GCC CAG TTT GAA GCA AAT GCT TTT GAA GCA Glu Leu Ile Asn Cys Ser Ala Gln Phe Glu Ala Asn Ala Phe Glu Ala 615 620 625	2109
50	CCA CTT ACA TTT GCA AAT GCT GAT TCA GGT TTA TTG CAT TCT TCT GTG Pro Leu Thr Phe Ala Asn Ala Asp Ser Gly Leu Leu His Ser Ser Val 630 635 640	2157
55	AAA AGA AGC TGT TCA CAG AAT GAT TCT GAA GAA CCA ACT TTG TCC TTA Lys Arg Ser Cys Ser Gln Asn Asp Ser Glu Glu Pro Thr Leu Ser Leu 645 650 655	2205
60	ACT AGC TCT TTT GGG ACA ATT CTG AGG AAA TGT TCT AGA AAT GAA ACA Thr Ser Ser Phe Gly Thr Ile Leu Arg Lys Cys Ser Arg Asn Glu Thr 660 665 670 675	2253
65	TGT TCT AAT AAT ACA GTA ATC TCT CAG GAT CTT GAT TAT AAA GAA GCA Cys Ser Asn Asn Thr Val Ile Ser Gln Asp Leu Asp Tyr Lys Glu Ala 680 685 690	2301
70	AAA TGT AAT AAG GAA AAA CTA CAG TTA TTT ATT ACC CCA GAA GCT GAT Lys Cys Asn Lys Glu Lys Leu Gln Leu Phe Ile Thr Pro Glu Ala Asp 695 700 705	2349
75	TCT CTG TCA TGC CTG CAG GAA GGA CAG TGT GAA AAT GAT CCA AAA AGC Ser Leu Ser Cys Leu Gln Glu Gly Gln Cys Glu Asn Asp Pro Lys Ser 710 715 720	2397

	AAA AAA GTT TCA GAT ATA AAA GAA GAG GTC TTG GCT GCA GCA TGT CAC	2445
	Lys Lys Val Ser Asp Ile Lys Glu Glu Val Leu Ala Ala Ala Cys His	
	725 730 735	
5	CCA GTA CAA CAT TCA AAA GTG GAA TAC AGT GAT ACT GAC TTT CAA TCC	2493
	Pro Val Gln His Ser Lys Val Glu Tyr Ser Asp Thr Asp Phe Gln Ser	
	740 745 750 755	
10	CAG AAA AGT CTT TTA TAT GAT CAT GAA AAT GCC AGC ACT CTT ATT TTA	2541
	Gln Lys Ser Leu Leu Tyr Asp His Glu Asn Ala Ser Thr Leu Ile Leu	
	760 765 770	
15	ACT CCT ACT TCC AAG GAT GTT CTG TCA AAC CTA GTC ATG ATT TCT AGA	2589
	Thr Pro Thr Ser Lys Asp Val Leu Ser Asn Leu Val Met Ile Ser Arg	
	775 780 785	
20	GGC AAA GAA TCA TAC AAA ATG TCA GAC AAG CTC AAA GGT AAC AAT TAT	2637
	Gly Lys Glu Ser Tyr Lys Met Ser Asp Lys Leu Lys Gly Asn Asn Tyr	
	790 795 800	
25	GAA TCT GAT GTT GAA TTA ACC AAA AAT ATT CCC ATG GAA AAG AAT CAA	2685
	Glu Ser Asp Val Glu Leu Thr Lys Asn Ile Pro Met Glu Lys Asn Gln	
	805 810 815	
30	GAT GTA TGT GCT TTA AAT GAA AAT TAT AAA AAC GTT GAG CTG TTG CCA	2733
	Asp Val Cys Ala Leu Asn Glu Asn Tyr Lys Asn Val Glu Leu Leu Pro	
	820 825 830 835	
35	CCT GAA AAA TAC ATG AGA GTA GCA TCA CCT TCA AGA AAG GTA CAA TTC	2781
	Pro Glu Lys Tyr Met Arg Val Ala Ser Pro Ser Arg Lys Val Gln Phe	
	840 845 850	
40	AAC CAA AAC ACA AAT CTA AGA GTA ATC CAA AAA AAT CAA GAA GAA ACT	2829
	Asn Gln Asn Thr Asn Leu Arg Val Ile Gln Lys Asn Gln Glu Glu Thr	
	855 860 865	
45	ACT TCA ATT TCA AAA ATA ACT GTC AAT CCA GAC TCT GAA GAA CTT TTC	2877
	Thr Ser Ile Ser Lys Ile Thr Val Asn Pro Asp Ser Glu Glu Leu Phe	
	870 875 880	
50	TCA GAC AAT GAG AAT AAT TTT GTC TTC CAA GTA GCT AAT GAA AGG AAT	2925
	Ser Asp Asn Glu Asn Asn Phe Val Phe Gln Val Ala Asn Glu Arg Asn	
	885 890 895	
55	AAT CTT GCT TTA GGA AAT ACT AAG GAA CTT CAT GAA ACA GAC TTG ACT	2973
	Asn Leu Ala Leu Gly Asn Thr Lys Glu Leu His Glu Thr Asp Leu Thr	
	900 905 910 915	
60	TGT GTA AAC GAA CCC ATT TTC AAG AAC TCT ACC ATG GTT TTA TAT GGA	3021
	Cys Val Asn Glu Pro Ile Phe Lys Asn Ser Thr Met Val Leu Tyr Gly	
	920 925 930	
65	GAC ACA GGT GAT AAA CAA GCA ACC CAA GTG TCA ATT AAA AAA GAT TTG	3069
	Asp Thr Gly Asp Lys Gln Ala Thr Gln Val Ser Ile Lys Lys Asp Leu	
	935 940 945	
70	GTT TAT GTT CTT GCA GAG GAG AAC AAA AAT AGT GTA AAG CAG CAT ATA	3117
	Val Tyr Val Leu Ala Glu Glu Asn Lys Asn Ser Val Lys Gln His Ile	
	950 955 960	
75	AAA ATG ACT CTA GGT CAA GAT TTA AAA TCG GAC ATC TCC TTG AAT ATA	3165

	Lys	Met	Thr	Leu	Gly	Gln	Asp	Leu	Lys	Ser	Asp	Ile	Ser	Leu	Asn	Ile	
	965						970					975					
5	GAT	AAA	ATA	CCA	GAA	AAA	AAT	AAT	GAT	TAC	ATG	AAC	AAA	TGG	GCA	GGA	3213
	Asp	Lys	Ile	Pro	Glu	Lys	Asn	Asn	Asp	Tyr	Met	Asn	Lys	Trp	Ala	Gly	
	980					985					990					995	
10	CTC	TTA	GGT	CCA	ATT	TCA	AAT	CAC	AGT	TTT	GGA	GGT	AGC	TTC	AGA	ACA	3261
	Leu	Leu	Gly	Pro	Ile	Ser	Asn	His	Ser	Phe	Gly	Gly	Ser	Phe	Arg	Thr	
					1000					1005					1010		
15	GCT	TCA	AAT	AAG	GAA	ATC	AAG	CTC	TCT	GAA	CAT	AAC	ATT	AAG	AAG	AGC	3309
	Ala	Ser	Asn	Lys	Glu	Ile	Lys	Leu	Ser	Glu	His	Asn	Ile	Lys	Lys	Ser	
				1015					1020					1025			
20	AAA	ATG	TTC	TTC	AAA	GAT	ATT	GAA	GAA	CAA	TAT	CCT	ACT	AGT	TTA	GCT	3357
	Lys	Met	Phe	Phe	Lys	Asp	Ile	Glu	Glu	Gln	Tyr	Pro	Thr	Ser	Leu	Ala	
			1030					1035					1040				
25	TGT	GTT	GAA	ATT	GTA	AAT	ACC	TTG	GCA	TTA	GAT	AAT	CAA	AAG	AAA	CTG	3405
	Cys	Val	Glu	Ile	Val	Asn	Thr	Leu	Ala	Leu	Asp	Asn	Gln	Lys	Lys	Leu	
		1045					1050					1055					
30	AGC	AAG	CCT	CAG	TCA	ATT	AAT	ACT	GTA	TCT	GCA	CAT	TTA	CAG	AGT	AGT	3453
	Ser	Lys	Pro	Gln	Ser	Ile	Asn	Thr	Val	Ser	Ala	His	Leu	Gln	Ser	Ser	
	1060					1065					1070				1075		
35	GTA	GTT	GTT	TCT	GAT	TGT	AAA	AAT	AGT	CAT	ATA	ACC	CCT	CAG	ATG	TTA	3501
	Val	Val	Val	Ser	Asp	Cys	Lys	Asn	Ser	His	Ile	Thr	Pro	Gln	Met	Leu	
					1080					1085					1090		
40	TTT	TCC	AAG	CAG	GAT	TTT	AAT	TCA	AAC	CAT	AAT	TTA	ACA	CCT	AGC	CAA	3549
	Phe	Ser	Lys	Gln	Asp	Phe	Asn	Ser	Asn	His	Asn	Leu	Thr	Pro	Ser	Gln	
				1095					1100					1105			
45	AAG	GCA	GAA	ATT	ACA	GAA	CTT	TCT	ACT	ATA	TTA	GAA	GAA	TCA	GGA	AGT	3597
	Lys	Ala	Glu	Ile	Thr	Glu	Leu	Ser	Thr	Ile	Leu	Glu	Glu	Ser	Gly	Ser	
			1110					1115					1120				
50	CAG	TTT	GAA	TTT	ACT	CAG	TTT	AGA	AAR	CCA	AGC	TAC	ATA	TTG	CAG	AAG	3645
	Gln	Phe	Glu	Phe	Thr	Gln	Phe	Arg	Xaa	Pro	Ser	Tyr	Ile	Leu	Gln	Lys	
		1125					1130					1135					
55	AGT	ACA	TTT	GAA	GTG	CCT	GAA	AAC	CAG	ATG	ACT	ATC	TTA	AAG	ACC	ACT	3693
	Ser	Thr	Phe	Glu	Val	Pro	Glu	Asn	Gln	Met	Thr	Ile	Leu	Lys	Thr	Thr	
	1140					1145					1150				1155		
60	TCT	GAG	GAA	TGC	AGA	GAT	GCT	GAT	CTT	CAT	GTC	ATA	ATG	AAT	GCC	CCA	3741
	Ser	Glu	Glu	Cys	Arg	Asp	Ala	Asp	Leu	His	Val	Ile	Met	Asn	Ala	Pro	
					1160					1165					1170		
65	TCG	ATT	GGT	CAG	GTA	GAC	AGC	AGC	AAG	CAA	TTT	GAA	GGT	ACA	GTT	GAA	3789
	Ser	Ile	Gly	Gln	Val	Asp	Ser	Ser	Lys	Gln	Phe	Glu	Gly	Thr	Val	Glu	
				1175					1180					1185			
70	ATT	AAA	CGG	AAG	TTT	GCT	GGC	CTG	TTG	AAA	AAT	GAC	TGT	AAC	AAA	AGT	3837
	Ile	Lys	Arg	Lys	Phe	Ala	Gly	Leu	Leu	Lys	Asn	Asp	Cys	Asn	Lys	Ser	
			1190				1195						1200				
75	GCT	TCT	GGT	TAT	TTA	ACA	GAT	GAA	AAT	GAA	GTG	GGG	TTT	AGG	GGC	TTT	3885
	Ala	Ser	Gly	Tyr	Leu	Thr	Asp	Glu	Asn	Glu	Val	Gly	Phe	Arg	Gly	Phe	

	1205	1210	1215	
5	TAT TCT GCT CAT GGC ACA AAA CTG AAT GTT TCT ACT GAA GCT CTG CAA Tyr Ser Ala His Gly Thr Lys Leu Asn Val Ser Thr Glu Ala Leu Gln 1220 1225 1230 1235	3933		
10	AAA GCT GTG AAA CTG TTT AGT GAT ATT GAG AAT ATT AGT GAG GAA ACT Lys Ala Val Lys Leu Phe Ser Asp Ile Glu Asn Ile Ser Glu Glu Thr 1240 1245 1250	3981		
15	TCT GCA GAG GTA CAT CCA ATA AGT TTA TCT TCA AGT AAA TGT CAT GAT Ser Ala Glu Val His Pro Ile Ser Leu Ser Ser Ser Lys Cys His Asp 1255 1260 1265	4029		
	TCT GTC GTT TCA ATG TTT AAG ATA GAA AAT CAT AAT GAT AAA ACT GTA Ser Val Val Ser Met Phe Lys Ile Glu Asn His Asn Asp Lys Thr Val 1270 1275 1280	4077		
20	AGT GAA AAA AAT AAT AAA TGC CAA CTG ATA TTA CAA AAT AAT ATT GAA Ser Glu Lys Asn Asn Lys Cys Gln Leu Ile Leu Gln Asn Asn Ile Glu 1285 1290 1295	4125		
25	ATG ACT ACT GGC ACT TTT GTT GAA GAA ATT ACT GAA AAT TAC AAG AGA Met Thr Thr Gly Thr Phe Val Glu Glu Ile Thr Glu Asn Tyr Lys Arg 1300 1305 1310 1315	4173		
30	AAT ACT GAA AAT GAA GAT AAC AAA TAT ACT GCT GCC AGT AGA AAT TCT Asn Thr Glu Asn Glu Asp Asn Lys Tyr Thr Ala Ala Ser Arg Asn Ser 1320 1325 1330	4221		
35	CAT AAC TTA GAA TTT GAT GGC AGT GAT TCA AGT AAA AAT GAT ACT GTT His Asn Leu Glu Phe Asp Gly Ser Asp Ser Ser Lys Asn Asp Thr Val 1335 1340 1345	4269		
	TGT ATT CAT AAA GAT GAA ACG GAC TTG CTA TTT ACT GAT CAG CAC AAC Cys Ile His Lys Asp Glu Thr Asp Leu Leu Phe Thr Asp Gln His Asn 1350 1355 1360	4317		
40	ATA TGT CTT AAA TTA TCT GGC CAG TTT ATG AAG GAG GGA AAC ACT CAG Ile Cys Leu Lys Leu Ser Gly Gln Phe Met Lys Glu Gly Asn Thr Gln 1365 1370 1375	4365		
45	ATT AAA GAA GAT TTG TCA GAT TTA ACT TTT TTG GAA GTT GCG AAA GCT Ile Lys Glu Asp Leu Ser Asp Leu Thr Phe Leu Glu Val Ala Lys Ala 1380 1385 1390 1395	4413		
50	CAA GAA GCA TGT CAT GGT AAT ACT TCA AAT AAA GAA CAG TTA ACT GCT Gln Glu Ala Cys His Gly Asn Thr Ser Asn Lys Glu Gln Leu Thr Ala 1400 1405 1410	4461		
	ACT AAA ACG GAG CAA AAT ATA AAA GAT TTT GAG ACT TCT GAT ACA TTT Thr Lys Thr Glu Gln Asn Ile Lys Asp Phe Glu Thr Ser Asp Thr Phe 1415 1420 1425	4509		
55	TTT CAG ACT GCA AGT GGG AAA AAT ATT AGT GTC GCC AAA GAG TCA TTT Phe Gln Thr Ala Ser Gly Lys Asn Ile Ser Val Ala Lys Glu Ser Phe 1430 1435 1440	4557		
60	AAT AAA ATT GTA AAT TTC TTT GAT CAG AAA CCA GAA GAA TTG CAT AAC Asn Lys Ile Val Asn Phe Phe Asp Gln Lys Pro Glu Glu Leu His Asn 1445 1450 1455	4605		

5	TTT TCC TTA AAT TCT GAA TTA CAT TCT GAC ATA AGA AAG AAC AAA ATG	4653
	Phe Ser Leu Asn Ser Glu Leu His Ser Asp Ile Arg Lys Asn Lys Met	
	1460 1465 1470 1475	
10	GAC ATT CTA AGT TAT GAG GAA ACA GAC ATA GTT AAA CAC AAA ATA CTG	4701
	Asp Ile Leu Ser Tyr Glu Glu Thr Asp Ile Val Lys His Lys Ile Leu	
	1480 1485 1490	
15	AAA GAA AGT GTC CCA GTT GGT ACT GGA AAT CAA CTA GTG ACC TTC CAG	4749
	Lys Glu Ser Val Pro Val Gly Thr Gly Asn Gln Leu Val Thr Phe Gln	
	1495 1500 1505	
20	GGA CAA CCC GAA CGT GAT GAA AAG ATC AAA GAA CCT ACT CTG TTG GGT	4797
	Gly Gln Pro Glu Arg Asp Glu Lys Ile Lys Glu Pro Thr Leu Leu Gly	
	1510 1515 1520	
25	TTT CAT ACA GCT AGC GGG AAA AAA GTT AAA ATT GCA AAG GAA TCT TTG	4845
	Phe His Thr Ala Ser Gly Lys Lys Val Lys Ile Ala Lys Glu Ser Leu	
	1525 1530 1535	
30	GAC AAA GTG AAA AAC CTT TTT GAT GAA AAA GAG CAA GGT ACT ACT GAA	4893
	Asp Lys Val Lys Asn Leu Phe Asp Glu Lys Glu Gln Gly Thr Ser Glu	
	1540 1545 1550 1555	
35	ATC ACC AGT TTT AGC CAT CAA TGG GCA AAG ACC CTA AAG TAC AGA GAG	4941
	Ile Thr Ser Phe Ser His Gln Trp Ala Lys Thr Leu Lys Tyr Arg Glu	
	1560 1565 1570	
40	GCC TGT AAA GAC CTT GAA TTA GCA TGT GAG ACC ATT GAG ATC ACA GCT	4989
	Ala Cys Lys Asp Leu Glu Leu Ala Cys Glu Thr Ile Glu Ile Thr Ala	
	1575 1580 1585	
45	GCC CCA AAG TGT AAA GAA ATG CAG AAT TCT CTC AAT AAT GAT AAA AAC	5037
	Ala Pro Lys Cys Lys Glu Met Gln Asn Ser Leu Asn Asn Asp Lys Asn	
	1590 1595 1600	
50	CTT GTT TCT ATT GAG ACT GTG GTG CCA CCT AAG CTC TTA AGT GAT AAT	5085
	Leu Val Ser Ile Glu Thr Val Val Pro Pro Lys Leu Leu Ser Asp Asn	
	1605 1610 1615	
55	TTA TGT AGA CAA ACT GAA AAT CTC AAA ACA TCA AAA AGT ATC TTT TTG	5133
	Leu Cys Arg Gln Thr Glu Asn Leu Lys Thr Ser Lys Ser Ile Phe Leu	
	1620 1625 1630 1635	
60	AAA GTT AAA GTA CAT GAA AAT GTA GAA AAA GAA ACA GCA AAA AGT CCT	5181
	Lys Val Lys Val Val Glu Asn Val Glu Lys Glu Thr Ala Lys Ser Pro	
	1640 1645 1650	
65	GCA ACT TGT TAC ACA AAT CAG TCC CCT TAT TCA GTC ATT GAA AAT TCA	5229
	Ala Thr Cys Tyr Thr Asn Gln Ser Pro Tyr Ser Val Ile Glu Asn Ser	
	1655 1660 1665	
70	GCC TTA GCT TTT TAC ACA AGT TGT AGT AGA AAA ACT TCT GTG AGT CAG	5277
	Ala Leu Ala Phe Tyr Thr Ser Cys Ser Arg Lys Thr Ser Val Ser Gln	
	1670 1675 1680	
75	ACT TCA TTA CTT GAA GCA AAA AAA TGG CTT AGA GAA GGA ATA TTT GAT	5325
	Thr Ser Leu Leu Glu Ala Lys Lys Trp Leu Arg Glu Gly Ile Phe Asp	
	1685 1690 1695	



	GGT CAA CCA GAA AGA ATA AAT ACT GCA GAT TAT GTA GGA AAT TAT TTG	5373
	Gly Gln Pro Glu Arg Ile Asn Thr Ala Asp Tyr Val Gly Asn Tyr Leu	
	1700 1705 1710 1715	
5	TAT GAA AAT AAT TCA AAC AGT ACT ATA GCT GAA AAT GAC AAA AAT CAT	5421
	Tyr Glu Asn Asn Ser Asn Ser Thr Ile Ala Glu Asn Asp Lys Asn His	
	1720 1725 1730	
10	CTC TCC GAA AAA CAA GAT ACT TAT TTA AGT AAC AGT AGC ATG TCT AAC	5469
	Leu Ser Glu Lys Gln Asp Thr Tyr Leu Ser Asn Ser Ser Met Ser Asn	
	1735 1740 1745	
15	AGC TAT TCC TAC CAT TCT GAT GAG GTA TAT AAT GAT TCA GGA TAT CTC	5517
	Ser Tyr Ser Tyr His Ser Asp Glu Val Tyr Asn Asp Ser Gly Tyr Leu	
	1750 1755 1760	
20	TCA AAA AAT AAA CTT GAT TCT GGT ATT GAG CCA GTA TTG AAG AAT GTT	5565
	Ser Lys Asn Lys Leu Asp Ser Gly Ile Glu Pro Val Leu Lys Asn Val	
	1765 1770 1775	
25	GAA GAT CAA AAA AAC ACT AGT TTT TCC AAA GTA ATA TCC AAT GTA AAA	5613
	Glu Asp Gln Lys Asn Thr Ser Phe Ser Lys Val Ile Ser Asn Val Lys	
	1780 1785 1790 1795	
	GAT GCA AAT GCA TAC CCA CAA ACT GTA AAT GAA GAT ATT TGC GTT GAG	5661
	Asp Ala Asn Ala Tyr Pro Gln Thr Val Asn Glu Asp Ile Cys Val Glu	
	1800 1805 1810	
30	GAA CTT GTG ACT AGC TCT TCA CCC TGC AAA AAT AAA AAT GCA GCC ATT	5709
	Glu Leu Val Thr Ser Ser Ser Pro Cys Lys Asn Lys Asn Ala Ala Ile	
	1815 1820 1825	
35	AAA TTG TCC ATA TCT AAT AGT AAT AAT TTT GAG GTA GGG CCA CCT GCA	5757
	Lys Leu Ser Ile Ser Asn Ser Asn Asn Phe Glu Val Gly Pro Pro Ala	
	1830 1835 1840	
40	TTT AGG ATA GCC AGT GGT AAA ATC GTT TGT GTT TCA CAT GAA ACA ATT	5805
	Phe Arg Ile Ala Ser Gly Lys Ile Val Cys Val Ser His Glu Thr Ile	
	1845 1850 1855	
45	AAA AAA GTG AAA GAC ATA TTT ACA GAC AGT TTC AGT AAA GTA ATT AAG	5853
	Lys Lys Val Lys Asp Ile Phe Thr Asp Ser Phe Ser Lys Val Ile Lys	
	1860 1865 1870 1875	
	GAA AAC AAC GAG AAT AAA TCA AAA ATT TGC CAA ACG AAA ATT ATG GCA	5901
	Glu Asn Asn Glu Asn Lys Ser Lys Ile Cys Gln Thr Lys Ile Met Ala	
	1880 1885 1890	
50	GGT TGT TAC GAG GCA TTG GAT GAT TCA GAG GAT ATT CTT CAT AAC TCT	5949
	Gly Cys Tyr Glu Ala Leu Asp Asp Ser Glu Asp Ile Leu His Asn Ser	
	1895 1900 1905	
55	CTA GAT AAT GAT GAA TGT AGC ACG CAT TCA CAT AAG GTT TTT GCT GAC	5997
	Leu Asp Asn Asp Glu Cys Ser Thr His Ser His Lys Val Phe Ala Asp	
	1910 1915 1920	
60	ATT CAG AGT GAA GAA ATT TTA CAA CAT AAC CAA AAT ATG TCT GGA TTG	6045
	Ile Gln Ser Glu Glu Ile Leu Gln His Asn Gln Asn Met Ser Gly Leu	
	1925 1930 1935	
	GAG AAA GTT TCT AAA ATA TCA CCT TGT GAT GTT AGT TTG GAA ACT TCA	6093

	Glu 1940	Lys	Val	Ser	Lys 1945	Ile	Ser	Pro	Cys	Asp	Val 1950	Ser	Leu	Glu	Thr	Ser 1955	
5	GAT Asp	ATA Ile	TGT Cys	AAA Lys	TGT Cys	AGT Ser	ATA Ile	GGG Gly	AAG Lys	CTT Leu	CAT His	AAG Lys	TCA Ser	GTC Val	TCA Ser	TCT Ser	6141
				1960					1965							1970	
10	GCA Ala	AAT Asn	ACT Thr	TGT Cys	GGG Gly	ATT Ile	TTT Phe	AGC Ser	ACA Thr	GCA Ala	AGT Ser	GGA Gly	AAA Lys	TCT Ser	GTC Val	CAG Gln	6189
				1975					1980							1985	
15	GTA Val	TCA Ser	GAT Asp	GCT Ala	TCA Ser	TTA Leu	CAA Gln	AAC Asn	GCA Ala	AGA Arg	CAA Gln	GTG Val	TTT Phe	TCT Ser	GAA Glu	ATA Ile	6237
				1990				1995					2000				
20	GAA Glu	GAT Asp	AGT Ser	ACC Thr	AAG Lys	CAA Gln	GTC Val	TTT Phe	TCC Ser	AAA Lys	GTA Val	TTG Leu	TTT Phe	AAA Lys	AGT Ser	AAC Asn	6285
				2005			2010					2015					
25	GAA Glu	CAT His	TCA Ser	GAC Asp	CAG Gln	CTC Leu	ACA Thr	AGA Arg	GAA Glu	GAA Glu	AAT Asn	ACT Thr	GCT Ala	ATA Ile	CGT Arg	ACT Thr	6333
	2020				2025						2030					2035	
30	CCA Pro	GAA Glu	CAT His	TTA Leu	ATA Ile	TCC Ser	CAA Gln	AAA Lys	GGC Gly	TTT Phe	TCA Ser	TAT Tyr	AAT Asn	GTG Val	GTA Val	AAT Asn	6381
					2040				2045						2050		
35	TCA Ser	TCT Ser	GCT Ala	TTC Phe	TCT Ser	GGA Gly	TTT Phe	AGT Ser	ACA Thr	GCA Ala	AGT Ser	GGA Gly	AAG Lys	CAA Gln	GTT Val	TCC Ser	6429
				2055				2060						2065			
40	ATT Ile	TTA Leu	GAA Glu	AGT Ser	TCC Ser	TTA Leu	CAC His	AAA Lys	GTT Val	AAG Lys	GGA Gly	GTG Val	TTA Leu	GAG Glu	GAA Glu	TTT Phe	6477
			2070				2075					2080					
45	GAT Asp	TTA Leu	ATC Ile	AGA Arg	ACT Thr	GAG Glu	CAT His	AGT Ser	CTT Leu	CAC His	TAT Tyr	TCA Ser	CCT Pro	ACG Thr	TCT Ser	AGA Arg	6525
	2085					2090					2095						
50	CAA Gln	AAT Asn	GTA Val	TCA Ser	AAA Lys	ATA Ile	CTT Leu	CCT Pro	CGT Arg	GTT Val	GAT Asp	AAG Lys	AGA Arg	AAC Asn	CCA Pro	GAG Glu	6573
	2100					2105				2110					2115		
55	CAC His	TGT Cys	GTA Val	AAC Asn	TCA Ser	GAA Glu	ATG Met	GAA Glu	AAA Lys	ACC Thr	TGC Cys	AGT Ser	AAA Lys	GAA Glu	TTT Phe	AAA Lys	6621
				2120				2125						2130			
60	TTA Leu	TCA Ser	AAT Asn	AAC Asn	TTA Leu	AAT Asn	GTT Val	GAA Glu	GGT Gly	GGT Gly	TCT Ser	TCA Ser	GAA Glu	AAT Asn	AAT Asn	CAC His	6669
			2135				2140						2145				
65	TCT Ser	ATT Ile	AAA Lys	GTT Val	TCT Ser	CCA Pro	TAT Tyr	CTC Leu	TCT Ser	CAA Gln	TTT Phe	CAA Gln	CAA Gln	GAC Asp	AAA Lys	CAA Gln	6717
			2150			2155					2160						
70	CAG Gln	TTG Leu	GTA Val	TTA Leu	GGA Gly	ACC Thr	AAA Lys	GTC Val	TCA Ser	CTT Leu	GTT Val	GAG Glu	AAC Asn	ATT Ile	CAT His	GTT Val	6765
	2165				2170						2175						
75	TTG Leu	GGA Gly	AAA Lys	GAA Glu	CAG Gln	GCT Ala	TCA Ser	CCT Pro	AAA Lys	AAC Asn	GTA Val	AAA Lys	ATG Met	GAA Glu	ATT Ile	GGT Gly	6813

	2180	2185	2190	2195	
5	AAA ACT GAA ACT TTT TCT GAT GTT CCT GTG AAA ACA AAT ATA GAA GTT Lys Thr Glu Thr Phe Ser Asp Val Pro Val Lys Thr Asn Ile Glu Val	2200	2205	2210	6861
10	TGT TCT ACT TAC TCC AAA GAT TCA GAA AAC TAC TTT GAA ACA GAA GCA Cys Ser Thr Tyr Ser Lys Asp Ser Glu Asn Tyr Phe Glu Thr Glu Ala	2215	2220	2225	6909
15	GTA GAA ATT GCT AAA GCT TTT ATG GAA GAT GAT GAA CTG ACA GAT TCT Val Glu Ile Ala Lys Ala Phe Met Glu Asp Asp Glu Leu Thr Asp Ser	2230	2235	2240	6957
	AAA CTG CCA AGT CAT GCC ACA CAT TCT CTT TTT ACA TGT CCC GAA AAT Lys Leu Pro Ser His Ala Thr His Ser Leu Phe Thr Cys Pro Glu Asn	2245	2250	2255	7005
20	GAG GAA ATG GTT TTG TCA AAT TCA AGA ATT GGA AAA AGA AGA GGA GAG Glu Glu Met Val Leu Ser Asn Ser Arg Ile Gly Lys Arg Arg Gly Glu	2260	2265	2270	7053
25	CCC CTT ATC TTA GTG GGA GAA CCC TCA ATC AAA AGA AAC TTA TTA AAT Pro Leu Ile Leu Val Gly Glu Pro Ser Ile Lys Arg Asn Leu Leu Asn	2280	2285	2290	7101
30	GAA TTT GAC AGG ATA ATA GAA AAT CAA GAA AAA TCC TTA AAG GCT TCA Glu Phe Asp Arg Ile Ile Glu Asn Gln Glu Lys Ser Leu Lys Ala Ser	2295	2300	2305	7149
35	AAA AGC ACT CCA GAT GGC ACA ATA AAA GAT CGA AGA TTG TTT ATG CAT Lys Ser Thr Pro Asp Gly Thr Ile Lys Asp Arg Arg Leu Phe Met His	2310	2315	2320	7197
	CAT GTT TCT TTA GAG CCG ATT ACC TGT GTA CCC TTT CGC ACA ACT AAG His Val Ser Leu Glu Pro Ile Thr Cys Val Pro Phe Arg Thr Thr Lys	2325	2330	2335	7245
40	GAA CGT CAA GAG ATA CAG AAT CCA AAT TTT ACC GCA CCT GGT CAA GAA Glu Arg Gln Glu Ile Gln Asn Pro Asn Phe Thr Ala Pro Gly Gln Glu	2340	2345	2350	7293
45	TTT CTG TCT AAA TCT CAT TTG TAT GAA CAT CTG ACT TTG GAA AAA TCT Phe Leu Ser Lys Ser His Leu Tyr Glu His Leu Thr Leu Glu Lys Ser	2360	2365	2370	7341
50	TCA AGC AAT TTA GCA GTT TCA GGA CAT CCA TTT TAT CAA GTT TCT GCT Ser Ser Asn Leu Ala Val Ser Gly His Pro Phe Tyr Gln Val Ser Ala	2375	2380	2385	7389
55	ACA AGA AAT GAA AAA ATG AGA CAC TTG ATT ACT ACA GGC AGA CCA ACC Thr Arg Asn Glu Lys Met Arg His Leu Ile Thr Thr Gly Arg Pro Thr	2390	2395	2400	7437
	AAA GTC TTT GTT CCA CCT TTT AAA ACT AAA TCA CAT TTT CAC AGA GTT Lys Val Phe Val Pro Pro Phe Lys Thr Lys Ser His Phe His Arg Val	2405	2410	2415	7485
60	GAA CAG TGT GTT AGG AAT ATT AAC TTG GAG GAA AAC AGA CAA AAG CAA Glu Gln Cys Val Arg Asn Ile Asn Leu Glu Glu Asn Arg Gln Lys Gln	2420	2425	2430	7533

5	AAC ATT GAT GGA CAT GGC TCT GAT GAT AGT AAA AAT AAG ATT AAT GAC Asn Ile Asp Gly His Gly Ser Asp Asp Ser Lys Asn Lys Ile Asn Asp 2440 2445 2450	7581
10	AAT GAG ATT CAT CAG TTT AAC AAA AAC AAC TCC AAT CAA GCA GCA GCT Asn Glu Ile His Gln Phe Asn Lys Asn Asn Ser Asn Gln Ala Ala Ala 2455 2460 2465	7629
15	GTA ACT TTC ACA AAG TGT GAA GAA GAA CCT TTA GAT TTA ATT ACA AGT Val Thr Phe Thr Lys Cys Glu Glu Glu Pro Leu Asp Leu Ile Thr Ser 2470 2475 2480	7677
20	CTT CAG AAT GCC AGA GAT ATA CAG GAT ATG CGA ATT AAG AAG AAA CAA Leu Gln Asn Ala Arg Asp Ile Gln Asp Met Arg Ile Lys Lys Lys Gln 2485 2490 2495	7725
25	AGG CAA CGC GTC TTT CCA CAG CCA GGC AGT CTG TAT CTT GCA AAA ACA Arg Gln Arg Val Phe Pro Gln Pro Gly Ser Leu Tyr Leu Ala Lys Thr 2500 2505 2510 2515	7773
30	TCC ACT CTG CCT CGA ATC TCT CTG AAA GCA GCA GTA GGA GGC CAA GTT Ser Thr Leu Pro Arg Ile Ser Leu Lys Ala Ala Val Gly Gly Gln Val 2520 2525 2530	7821
35	CCC TCT GCG TGT TCT CAT AAA CAG CTG TAT ACG TAT GGC GTT TCT AAA Pro Ser Ala Cys Ser His Lys Gln Leu Tyr Thr Tyr Gly Val Ser Lys 2535 2540 2545	7869
40	CAT TGC ATA AAA ATT AAC AGC AAA AAT GCA GAG TCT TTT CAG TTT CAC His Cys Ile Lys Ile Asn Ser Lys Asn Ala Glu Ser Phe Gln Phe His 2550 2555 2560	7917
45	ACT GAA GAT TAT TTT GGT AAG GAA AGT TTA TGG ACT GGA AAA GGA ATA Thr Glu Asp Tyr Phe Gly Lys Glu Ser Leu Trp Thr Gly Lys Gly Ile 2565 2570 2575	7965
50	CAG TTG GCT GAT GGT GGA TGG CTC ATA CCC TCC AAT GAT GGA AAG GCT Gln Leu Ala Asp Gly Gly Trp Leu Ile Pro Ser Asn Asp Gly Lys Ala 2580 2585 2590 2595	8013
55	GGA AAA GAA GAA TTT TAT AGG GCT CTG TGT GAC ACT CCA GGT GTG GAT Gly Lys Glu Glu Phe Tyr Arg Ala Leu Cys Asp Thr Pro Gly Val Asp 2600 2605 2610	8061
60	CCA AAG CTT ATT TCT AGA ATT TGG GTT TAT AAT CAC TAT AGA TGG ATC Pro Lys Leu Ile Ser Arg Ile Trp Val Tyr Asn His Tyr Arg Trp Ile 2615 2620 2625	8109
65	ATA TGG AAA CTG GCA GCT ATG GAA TGT GCC TTT CCT AAG GAA TTT GCT Ile Trp Lys Leu Ala Ala Met Glu Cys Ala Phe Pro Lys Glu Phe Ala 2630 2635 2640	8157
70	AAT AGA TGC CTA AGC CCA GAA AGG GTG CTT CTT CAA CTA AAA TAC AGA Asn Arg Cys Leu Ser Pro Glu Arg Val Leu Leu Gln Leu Lys Tyr Arg 2645 2650 2655	8205
75	TAT GAT ACG GAA ATT GAT AGA AGC AGA AGA TCG GCT ATA AAA AAG ATA Tyr Asp Thr Glu Ile Asp Arg Ser Arg Arg Ser Ala Ile Lys Lys Ile 2660 2665 2670 2675	8253

	ATG GAA AGG GAT GAC ACA GCT GCA AAA ACA CTT GTT CTC TGT GTT TCT	8301
	Met Glu Arg Asp Asp Thr Ala Ala Lys Thr Leu Val Leu Cys Val Ser	
	2680 2685 2690	
5	GAC ATA ATT TCA TTG AGC GCA AAT ATA TCT GAA ACT TCT AGC AAT AAA	8349
	Asp Ile Ile Ser Leu Ser Ala Asn Ile Ser Glu Thr Ser Ser Asn Lys	
	2695 2700 2705	
10	ACT AGT AGT GCA GAT ACC CAA AAA GTG GCC ATT ATT GAA CTT ACA GAT	8397
	Thr Ser Ser Ala Asp Thr Gln Lys Val Ala Ile Ile Glu Leu Thr Asp	
	2710 2715 2720	
15	GGG TGG TAT GCT GTT AAG GCC CAG TTA GAT CCT CCC CTC TTA GCT GTC	8445
	Gly Trp Tyr Ala Val Lys Ala Gln Leu Asp Pro Pro Leu Leu Ala Val	
	2725 2730 2735	
20	TTA AAG AAT GGC AGA CTG ACA GTT GGT CAG AAG ATT ATT CTT CAT GGA	8493
	Leu Lys Asn Gly Arg Leu Thr Val Gly Gln Lys Ile Ile Leu His Gly	
	2740 2745 2750 2755	
25	GCA GAA CTG GTG GGC TCT CCT GAT GCC TGT ACA CCT CTT GAA GCC CCA	8541
	Ala Glu Leu Val Gly Ser Pro Asp Ala Cys Thr Pro Leu Glu Ala Pro	
	2760 2765 2770	
	GAA TCT CTT ATG TTA AAG ATT TCT GCT AAC AGT ACT CGG CCT GCT CGC	8589
	Glu Ser Leu Met Leu Lys Ile Ser Ala Asn Ser Thr Arg Pro Ala Arg	
	2775 2780 2785	
30	TGG TAT ACC AAA CTT GGA TTC TTT CCT GAC CCT AGA CCT TTT CCT CTG	8637
	Trp Tyr Thr Lys Leu Gly Phe Phe Pro Asp Pro Arg Pro Phe Pro Leu	
	2790 2795 2800	
35	CCC TTA TCA TCG CTT TTC AGT GAT GGA GGA AAT GTT GGT TGT GTT GAT	8685
	Pro Leu Ser Ser Leu Phe Ser Asp Gly Gly Asn Val Gly Cys Val Asp	
	2805 2810 2815	
40	GTA ATT ATT CAA AGA GCA TAC CCT ATA CAG TGG ATG GAG AAG ACA TCA	8733
	Val Ile Ile Gln Arg Ala Tyr Pro Ile Gln Trp Met Glu Lys Thr Ser	
	2820 2825 2830 2835	
45	TCT GGA TTA TAC ATA TTT CGC AAT GAA AGA GAG GAA GAA AAG GAA GCA	8781
	Ser Gly Leu Tyr Ile Phe Arg Asn Glu Arg Glu Glu Glu Lys Glu Ala	
	2840 2845 2850	
	GCA AAA TAT GTG GAG GCC CAA CAA AAG AGA CTA GAA GCC TTA TTC ACT	8829
	Ala Lys Tyr Val Glu Ala Gln Gln Lys Arg Leu Glu Ala Leu Phe Thr	
	2855 2860 2865	
50	AAA ATT CAG GAG GAA TTT GAA GAA CAT GAA GAA AAC ACA ACA AAA CCA	8877
	Lys Ile Gln Glu Glu Phe Glu Glu His Glu Glu Asn Thr Thr Lys Pro	
	2870 2875 2880	
55	TAT TTA CCA TCA CGT GCA CTA ACA AGA CAG CAA GTT CGT GCT TTG CAA	8925
	Tyr Leu Pro Ser Arg Ala Leu Thr Arg Gln Gln Val Arg Ala Leu Gln	
	2885 2890 2895	
60	GAT GGT GCA GAG CTT TAT GAA GCA GTG AAG AAT GCA GCA GAC CCA GCT	8973
	Asp Gly Ala Glu Leu Tyr Glu Ala Val Lys Asn Ala Ala Asp Pro Ala	
	2900 2905 2910 2915	
	TAC CTT GAG GGT TAT TTC AGT GAA GAG CAG TTA AGA GCC TTG AAT AAT	9021

	Tyr	Leu	Glu	Gly	Tyr	Phe	Ser	Glu	Glu	Gln	Leu	Arg	Ala	Leu	Asn	Asn	
					2920					2925					2930		
5	CAC	AGG	CAA	ATG	TTG	AAT	GAT	AAG	AAA	CAA	GCT	CAG	ATC	CAG	TTG	GAA	9069
	His	Arg	Gln	Met	Leu	Asn	Asp	Lys	Lys	Gln	Ala	Gln	Ile	Gln	Leu	Glu	
				2935					2940					2945			
10	ATT	AGG	AAG	GCC	ATG	GAA	TCT	GCT	GAA	CAA	AAG	GAA	CAA	GGT	TTA	TCA	9117
	Ile	Arg	Lys	Ala	Met	Glu	Ser	Ala	Glu	Gln	Lys	Glu	Gln	Gly	Leu	Ser	
			2950					2955						2960			
15	AGG	GAT	GTC	ACA	ACC	GTG	TGG	AAG	TTG	CGT	ATT	GTA	AGC	TAT	TCA	AAA	9165
	Arg	Asp	Val	Thr	Thr	Val	Trp	Lys	Leu	Arg	Ile	Val	Ser	Tyr	Ser	Lys	
		2965					2970					2975					
20	AAA	GAA	AAA	GAT	TCA	GTT	ATA	CTG	AGT	ATT	TGG	CGT	CCA	TCA	TCA	GAT	9213
	Lys	Glu	Lys	Asp	Ser	Val	Ile	Leu	Ser	Ile	Trp	Arg	Pro	Ser	Ser	Asp	
	2980					2985					2990					2995	
	TTA	TAT	TCT	CTG	TTA	ACA	GAA	GGA	AAG	AGA	TAC	AGA	ATT	TAT	CAT	CTT	9261
	Leu	Tyr	Ser	Leu	Leu	Thr	Glu	Gly	Lys	Arg	Tyr	Arg	Ile	Tyr	His	Leu	
				3000						3005					3010		
25	GCA	ACT	TCA	AAA	TCT	AAA	AGT	AAA	TCT	GAA	AGA	GCT	AAC	ATA	CAG	TTA	9309
	Ala	Thr	Ser	Lys	Ser	Lys	Ser	Lys	Ser	Glu	Arg	Ala	Asn	Ile	Gln	Leu	
				3015					3020					3025			
30	GCA	GCG	ACA	AAA	AAA	ACT	CAG	TAT	CAA	CAA	CTA	CCG	GTT	TCA	GAT	GAA	9357
	Ala	Ala	Thr	Lys	Lys	Thr	Gln	Tyr	Gln	Gln	Leu	Pro	Val	Ser	Asp	Glu	
			3030				3035						3040				
35	ATT	TTA	TTT	CAG	ATT	TAC	CAG	CCA	CGG	GAG	CCC	CTT	CAC	TTC	AGC	AAA	9405
	Ile	Leu	Phe	Gln	Ile	Tyr	Gln	Pro	Arg	Glu	Pro	Leu	His	Phe	Ser	Lys	
		3045				3050					3055						
40	TTT	TTA	GAT	CCA	GAC	TTT	CAG	CCA	TCT	TGT	TCT	GAG	GTG	GAC	CTA	ATA	9453
	Phe	Leu	Asp	Pro	Asp	Phe	Gln	Pro	Ser	Cys	Ser	Glu	Val	Asp	Leu	Ile	
	3060				3065					3070					3075		
	GGA	TTT	GTC	GTT	TCT	GTT	GTG	AAA	AAA	ACA	GGA	CTT	GCC	CCT	TTC	GTC	9501
	Gly	Phe	Val	Val	Ser	Val	Val	Lys	Lys	Thr	Gly	Leu	Ala	Pro	Phe	Val	
				3080					3085					3090			
45	TAT	TTG	TCA	GAC	GAA	TGT	TAC	AAT	TTA	CTG	GCA	ATA	AAG	TTT	TGG	ATA	9549
	Tyr	Leu	Ser	Asp	Glu	Cys	Tyr	Asn	Leu	Leu	Ala	Ile	Lys	Phe	Trp	Ile	
				3095				3100					3105				
50	GAC	CTT	AAT	GAG	GAC	ATT	ATT	AAG	CCT	CAT	ATG	TTA	ATT	GCT	GCA	AGC	9597
	Asp	Leu	Asn	Glu	Asp	Ile	Ile	Lys	Pro	His	Met	Leu	Ile	Ala	Ala	Ser	
		3110					3115					3120					
55	AAC	CTC	CAG	TGG	CGA	CCA	GAA	TCC	AAA	TCA	GGC	CTT	CTT	ACT	TTA	TTT	9645
	Asn	Leu	Gln	Trp	Arg	Pro	Glu	Ser	Lys	Ser	Gly	Leu	Leu	Thr	Leu	Phe	
		3125				3130					3135						
60	GCT	GGA	GAT	TTT	TCT	GTG	TTT	TCT	GCT	AGT	CCA	AAA	GAG	GGC	CAC	TTT	9693
	Ala	Gly	Asp	Phe	Ser	Val	Phe	Ser	Ala	Ser	Pro	Lys	Glu	Gly	His	Phe	
	3140				3145					3150				3155			
	CAA	GAG	ACA	TTC	AAC	AAA	ATG	AAA	AAT	ACT	GTT	GAG	AAT	ATT	GAC	ATA	9741
	Gln	Glu	Thr	Phe	Asn	Lys	Met	Lys	Asn	Thr	Val	Glu	Asn	Ile	Asp	Ile	

	3160	3165	3170	
5	CTT TGC AAT GAA GCA GAA AAC AAG CTT ATG CAT ATA CTG CAT GCA AAT Leu Cys Asn Glu Ala Glu Asn Lys Leu Met His Ile Leu His Ala Asn 3175 3180 3185	9789		
10	GAT CCC AAG TGG TCC ACC CCA ACT AAA GAC TGT ACT TCA GGG CCG TAC Asp Pro Lys Trp Ser Thr Pro Thr Lys Asp Cys Thr Ser Gly Pro Tyr 3190 3195 3200	9837		
15	ACT GCT CAA ATC ATT CCT GGT ACA GGA AAC AAG CTT CTG ATG TCT TCT Thr Ala Gln Ile Ile Pro Gly Thr Gly Asn Lys Leu Leu Met Ser Ser 3205 3210 3215	9885		
20	CCT AAT TGT GAG ATA TAT TAT CAA AGT CCT TTA TCA CTT TGT ATG GCC Pro Asn Cys Glu Ile Tyr Tyr Gln Ser Pro Leu Ser Leu Cys Met Ala 3220 3225 3230 3235	9933		
25	AAA AGG AAG TCT GTT TCC ACA CCT GTC TCA GCC CAG ATG ACT TCA AAG Lys Arg Lys Ser Val Ser Thr Pro Val Ser Ala Gln Met Thr Ser Lys 3240 3245 3250	9981		
30	TCT TGT AAA GGG GAG AAA GAG ATT GAT GAC CAA AAG AAC TGC AAA AAG Ser Cys Lys Gly Glu Lys Glu Ile Asp Asp Gln Lys Asn Cys Lys Lys 3255 3260 3265	10029		
35	AGA AGA GCC TTG GAT TTC TTG AGT AGA CTG CCT TTA CCT CCA CCT GTT Arg Arg Ala Leu Asp Phe Leu Ser Arg Leu Pro Leu Pro Pro Pro Val 3270 3275 3280	10077		
40	AGT CCC ATT TGT ACA TTT GTT TCT CCG GCT GCA CAG AAG GCA TTT CAG Ser Pro Ile Cys Thr Phe Val Ser Pro Ala Ala Gln Lys Ala Phe Gln 3285 3290 3295	10125		
45	CCA CCA AGG AGT TGT GGC ACC AAA TAC GAA ACA CCC ATA AAG AAA AAA Pro Pro Arg Ser Cys Gly Thr Lys Tyr Glu Thr Pro Ile Lys Lys Lys 3300 3305 3310 3315	10173		
50	GAA CTG AAT TCT CCT CAG ATG ACT CCA TTT AAA AAA TTC AAT GAA ATT Glu Leu Asn Ser Pro Gln Met Thr Pro Phe Lys Lys Phe Asn Glu Ile 3320 3325 3330	10221		
55	TCT CTT TTG GAA AGT AAT TCA ATA GCT GAC GAA GAA CTT GCA TTG ATA Ser Leu Leu Glu Ser Asn Ser Ile Ala Asp Glu Glu Leu Ala Leu Ile 3335 3340 3345	10269		
60	AAT ACC CAA GCT CTT TTG TCT GGT TCA ACA GGA GAA AAA CAA TTT ATA Asn Thr Gln Ala Leu Leu Ser Gly Ser Lys Gly Glu Lys Gln Phe Ile 3350 3355 3360	10317		
65	TCT GTC AGT GAA TCC ACT AGG ACT GCT CCC ACC AGT TCA GAA GAT TAT Ser Val Ser Glu Ser Thr Arg Thr Ala Pro Thr Ser Ser Glu Asp Tyr 3365 3370 3375	10365		
70	CTC AGA CTG AAA CGA CGT TGT ACT ACA TCT CTG ATC AAA GAA CAG GAG Leu Arg Leu Lys Arg Arg Cys Thr Thr Ser Leu Ile Lys Glu Gln Glu 3380 3385 3390 3395	10413		
75	AGT TCC CAG GCC AGT ACG GAA GAA TGT GAG AAA AAT AAG CAG GAC ACA Ser Ser Gln Ala Ser Thr Glu Glu Cys Glu Lys Asn Lys Gln Asp Thr 3400 3405 3410	10461		

ATT ACA ACT AAA AAA TAT ATC TAA  
 Ile Thr Thr Lys Lys Tyr Ile  
 3415

10485

5

## (2) INFORMATION FOR SEQ ID NO:7:

10

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 3418 amino acids  
 (B) TYPE: amino acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

15

- (ii) MOLECULE TYPE: protein  
 (v) FRAGMENT TYPE: internal

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

20

Met	Pro	Ile	Gly	Ser	Lys	Glu	Arg	Pro	Thr	Phe	Phe	Glu	Ile	Phe	Lys
1				5					10					15	
Thr	Arg	Cys	Asn	Lys	Ala	Asp	Leu	Gly	Pro	Ile	Ser	Leu	Asn	Trp	Phe
			20					25					30		
25	Glu	Glu	Leu	Ser	Ser	Glu	Ala	Pro	Pro	Tyr	Asn	Ser	Glu	Pro	Ala
			35					40					45		
Glu	Ser	Glu	His	Lys	Asn	Asn	Asn	Tyr	Glu	Pro	Asn	Leu	Phe	Lys	Thr
			50			55					60				
Pro	Gln	Arg	Lys	Pro	Ser	Tyr	Asn	Gln	Leu	Ala	Ser	Thr	Pro	Ile	Ile
						70				75				80	
30	Phe	Lys	Glu	Gln	Gly	Leu	Thr	Leu	Pro	Leu	Tyr	Gln	Ser	Pro	Val
				85					90					95	
Glu	Leu	Asp	Lys	Phe	Lys	Leu	Asp	Leu	Gly	Arg	Asn	Val	Pro	Asn	Ser
			100					105					110		
35	Arg	His	Lys	Ser	Leu	Arg	Thr	Val	Lys	Thr	Lys	Met	Asp	Gln	Ala
			115					120					125		
Asp	Val	Ser	Cys	Pro	Leu	Leu	Asn	Ser	Cys	Leu	Ser	Glu	Ser	Pro	Val
			130			135					140				
Val	Leu	Gln	Cys	Thr	His	Val	Thr	Pro	Gln	Arg	Asp	Lys	Ser	Val	Val
					150					155				160	
40	Cys	Gly	Ser	Leu	Phe	His	Thr	Pro	Lys	Phe	Val	Lys	Gly	Arg	Gln
				165						170				175	
Pro	Lys	His	Ile	Ser	Glu	Ser	Leu	Gly	Ala	Glu	Val	Asp	Pro	Asp	Met
			180					185					190		
45	Ser	Trp	Ser	Ser	Ser	Leu	Ala	Thr	Pro	Pro	Thr	Leu	Ser	Ser	Thr
			195					200					205		
Leu	Ile	Val	Arg	Asn	Glu	Glu	Ala	Ser	Glu	Thr	Val	Phe	Pro	His	Asp
			210			215					220				
Thr	Thr	Ala	Asn	Val	Lys	Ser	Tyr	Phe	Ser	Asn	His	Asp	Glu	Ser	Leu
					230					235				240	
50	Lys	Lys	Asn	Asp	Arg	Phe	Ile	Ala	Ser	Val	Thr	Asp	Ser	Glu	Asn
				245						250				255	
Asn	Gln	Arg	Glu	Ala	Ala	Ser	His	Gly	Phe	Gly	Lys	Thr	Ser	Gly	Asn
			260					265					270		
55	Ser	Phe	Lys	Val	Asn	Ser	Cys	Lys	Asp	His	Ile	Gly	Lys	Ser	Met
			275					280					285		
Asn	Val	Leu	Glu	Asp	Glu	Val	Tyr	Glu	Thr	Val	Val	Asp	Thr	Ser	Glu
			290			295					300				
Glu	Asp	Ser	Phe	Ser	Leu	Cys	Phe	Ser	Lys	Cys	Arg	Thr	Lys	Asn	Leu
					310					315				320	
60	Gln	Lys	Val	Arg	Thr	Ser	Lys	Thr	Arg	Lys	Lys	Ile	Phe	His	Glu
					325				330					335	



Asn Ala Asp Glu Cys Glu Lys Ser Lys Asn Gln Val Lys Glu Lys Tyr  
 340 345 350  
 Ser Phe Val Ser Glu Val Glu Pro Asn Asp Thr Asp Pro Leu Asp Ser  
 355 360 365  
 5 Asn Val Ala His Gln Lys Pro Phe Glu Ser Gly Ser Asp Lys Ile Ser  
 370 375 380  
 Lys Glu Val Val Pro Ser Leu Ala Cys Glu Trp Ser Gln Leu Thr Leu  
 385 390 395 400  
 10 Ser Gly Leu Asn Gly Ala Gln Met Glu Lys Ile Pro Leu Leu His Ile  
 405 410 415  
 Ser Ser Cys Asp Gln Asn Ile Ser Glu Lys Asp Leu Leu Asp Thr Glu  
 420 425 430  
 Asn Lys Arg Lys Lys Asp Phe Leu Thr Ser Glu Asn Ser Leu Pro Arg  
 435 440 445  
 15 Ile Ser Ser Leu Pro Lys Ser Glu Lys Pro Leu Asn Glu Glu Thr Val  
 450 455 460  
 Val Asn Lys Arg Asp Glu Glu Gln His Leu Glu Ser His Thr Asp Cys  
 465 470 475 480  
 20 Ile Leu Ala Val Lys Gln Ala Ile Ser Gly Thr Ser Pro Val Ala Ser  
 485 490 495  
 Ser Phe Gln Gly Ile Lys Lys Ser Ile Phe Arg Ile Arg Glu Ser Pro  
 500 505 510  
 Lys Glu Thr Phe Asn Ala Ser Phe Ser Gly His Met Thr Asp Pro Asn  
 515 520 525  
 25 Phe Lys Lys Glu Thr Glu Ala Ser Glu Ser Gly Leu Glu Ile His Thr  
 530 535 540  
 Val Cys Ser Gln Lys Glu Asp Ser Leu Cys Pro Asn Leu Ile Asp Asn  
 545 550 555 560  
 30 Gly Ser Trp Pro Ala Thr Thr Thr Gln Asn Ser Val Ala Leu Lys Asn  
 565 570 575  
 Ala Gly Leu Ile Ser Thr Leu Lys Lys Lys Thr Asn Lys Phe Ile Tyr  
 580 585 590  
 Ala Ile His Asp Glu Thr Ser Tyr Lys Gly Lys Lys Ile Pro Lys Asp  
 595 600 605  
 35 Gln Lys Ser Glu Leu Ile Asn Cys Ser Ala Gln Phe Glu Ala Asn Ala  
 610 615 620  
 Phe Glu Ala Pro Leu Thr Phe Ala Asn Ala Asp Ser Gly Leu Leu His  
 625 630 635 640  
 40 Ser Ser Val Lys Arg Ser Cys Ser Gln Asn Asp Ser Glu Glu Pro Thr  
 645 650 655  
 Leu Ser Leu Thr Ser Ser Phe Gly Thr Ile Leu Arg Lys Cys Ser Arg  
 660 665 670  
 Asn Glu Thr Cys Ser Asn Asn Thr Val Ile Ser Gln Asp Leu Asp Tyr  
 675 680 685  
 45 Lys Glu Ala Lys Cys Asn Lys Glu Lys Leu Gln Leu Phe Ile Thr Pro  
 690 695 700  
 Glu Ala Asp Ser Leu Ser Cys Leu Gln Glu Gly Gln Cys Glu Asn Asp  
 705 710 715 720  
 50 Pro Lys Ser Lys Lys Val Ser Asp Ile Lys Glu Glu Val Leu Ala Ala  
 725 730 735  
 Ala Cys His Pro Val Gln His Ser Lys Val Glu Tyr Ser Asp Thr Asp  
 740 745 750  
 Phe Gln Ser Gln Lys Ser Leu Leu Tyr Asp His Glu Asn Ala Ser Thr  
 755 760 765  
 55 Leu Ile Leu Thr Pro Thr Ser Lys Asp Val Leu Ser Asn Leu Val Met  
 770 775 780  
 Ile Ser Arg Gly Lys Glu Ser Tyr Lys Met Ser Asp Lys Leu Lys Gly  
 785 790 795 800  
 60 Asn Asn Tyr Glu Ser Asp Val Glu Leu Thr Lys Asn Ile Pro Met Glu  
 805 810 815  
 Lys Asn Gln Asp Val Cys Ala Leu Asn Glu Asn Tyr Lys Asn Val Glu

92

Tyr Lys Arg Asn Thr Glu Asn Glu Asp Asn Lys Tyr Thr Ala Ala Ser  
 1315 1320 1325  
 5 Arg Asn Ser His Asn Leu Glu Phe Asp Gly Ser Asp Ser Ser Lys Asn  
 1330 1335 1340  
 Asp Thr Val Cys Ile His Lys Asp Glu Thr Asp Leu Leu Phe Thr Asp  
 1345 1350 1355 136  
 Gln His Asn Ile Cys Leu Lys Leu Ser Gly Gln Phe Met Lys Glu Gly  
 1365 1370 1375  
 10 Asn Thr Gln Ile Lys Glu Asp Leu Ser Asp Leu Thr Phe Leu Glu Val  
 1380 1385 1390  
 Ala Lys Ala Gln Glu Ala Cys His Gly Asn Thr Ser Asn Lys Glu Gln  
 1395 1400 1405  
 Leu Thr Ala Thr Lys Thr Glu Gln Asn Ile Lys Asp Phe Glu Thr Ser  
 1410 1415 1420  
 15 Asp Thr Phe Phe Gln Thr Ala Ser Gly Lys Asn Ile Ser Val Ala Lys  
 1425 1430 1435 144  
 Glu Ser Phe Asn Lys Ile Val Asn Phe Phe Asp Gln Lys Pro Glu Glu  
 1445 1450 1455  
 20 Leu His Asn Phe Ser Leu Asn Ser Glu Leu His Ser Asp Ile Arg Lys  
 1460 1465 1470  
 Asn Lys Met Asp Ile Leu Ser Tyr Glu Glu Thr Asp Ile Val Lys His  
 1475 1480 1485  
 Lys Ile Leu Lys Glu Ser Val Pro Val Gly Thr Gly Asn Gln Leu Val  
 1490 1495 1500  
 25 Thr Phe Gln Gly Gln Pro Glu Arg Asp Glu Lys Ile Lys Glu Pro Thr  
 1505 1510 1515 152  
 Leu Leu Gly Phe His Thr Ala Ser Gly Lys Lys Val Lys Ile Ala Lys  
 1525 1530 1535  
 30 Glu Ser Leu Asp Lys Val Lys Asn Leu Phe Asp Glu Lys Glu Gln Gly  
 1540 1545 1550  
 Thr Ser Glu Ile Thr Ser Phe Ser His Gln Trp Ala Lys Thr Leu Lys  
 1555 1560 1565  
 Tyr Arg Glu Ala Cys Lys Asp Leu Glu Leu Ala Cys Glu Thr Ile Glu  
 1570 1575 1580  
 35 Ile Thr Ala Ala Pro Lys Cys Lys Glu Met Gln Asn Ser Leu Asn Asn  
 1585 1590 1595 160  
 Asp Lys Asn Leu Val Ser Ile Glu Thr Val Val Pro Pro Lys Leu Leu  
 1605 1610 1615  
 40 Ser Asp Asn Leu Cys Arg Gln Thr Glu Asn Leu Lys Thr Ser Lys Ser  
 1620 1625 1630  
 Ile Phe Leu Lys Val Lys Val His Glu Asn Val Glu Lys Glu Thr Ala  
 1635 1640 1645  
 Lys Ser Pro Ala Thr Cys Tyr Thr Asn Gln Ser Pro Tyr Ser Val Ile  
 1650 1655 1660  
 45 Glu Asn Ser Ala Leu Ala Phe Tyr Thr Ser Cys Ser Arg Lys Thr Ser  
 1665 1670 1675 168  
 Val Ser Gln Thr Ser Leu Leu Glu Ala Lys Lys Trp Leu Arg Glu Gly  
 1685 1690 1695  
 50 Ile Phe Asp Gly Gln Pro Glu Arg Ile Asn Thr Ala Asp Tyr Val Gly  
 1700 1705 1710  
 Asn Tyr Leu Tyr Glu Asn Asn Ser Asn Ser Thr Ile Ala Glu Asn Asp  
 1715 1720 1725  
 Lys Asn His Leu Ser Glu Lys Gln Asp Thr Tyr Leu Ser Asn Ser Ser  
 1730 1735 1740  
 55 Met Ser Asn Ser Tyr Ser Tyr His Ser Asp Glu Val Tyr Asn Asp Ser  
 1745 1750 1755 176  
 Gly Tyr Leu Ser Lys Asn Lys Leu Asp Ser Gly Ile Glu Pro Val Leu  
 1765 1770 1775  
 60 Lys Asn Val Glu Asp Gln Lys Asn Thr Ser Phe Ser Lys Val Ile Ser  
 1780 1785 1790  
 Asn Val Lys Asp Ala Asn Ala Tyr Pro Gln Thr Val Asn Glu Asp Ile

	1795	1800	1805
	Cys Val Glu Glu Leu Val Thr Ser Ser Ser Pro Cys Lys Asn Lys Asn		
	1810	1815	1820
5	Ala Ala Ile Lys Leu Ser Ile Ser Asn Ser Asn Asn Phe Glu Val Gly		
	1825	1830	1835
	Pro Pro Ala Phe Arg Ile Ala Ser Gly Lys Ile Val Cys Val Ser His		
	1845	1850	1855
10	Glu Thr Ile Lys Lys Val Lys Asp Ile Phe Thr Asp Ser Phe Ser Lys		
	1860	1865	1870
	Val Ile Lys Glu Asn Asn Glu Asn Lys Ser Lys Ile Cys Gln Thr Lys		
	1875	1880	1885
	Ile Met Ala Gly Cys Tyr Glu Ala Leu Asp Asp Ser Glu Asp Ile Leu		
	1890	1895	1900
15	His Asn Ser Leu Asp Asn Asp Glu Cys Ser Thr His Ser His Lys Val		
	1905	1910	1915
	Phe Ala Asp Ile Gln Ser Glu Glu Ile Leu Gln His Asn Gln Asn Met		
	1925	1930	1935
20	Ser Gly Leu Glu Lys Val Ser Lys Ile Ser Pro Cys Asp Val Ser Leu		
	1940	1945	1950
	Glu Thr Ser Asp Ile Cys Lys Cys Ser Ile Gly Lys Leu His Lys Ser		
	1955	1960	1965
	Val Ser Ser Ala Asn Thr Cys Gly Ile Phe Ser Thr Ala Ser Gly Lys		
	1970	1975	1980
25	Ser Val Gln Val Ser Asp Ala Ser Leu Gln Asn Ala Arg Gln Val Phe		
	1985	1990	1995
	Ser Glu Ile Glu Asp Ser Thr Lys Gln Val Phe Ser Lys Val Leu Phe		
	2005	2010	2015
30	Lys Ser Asn Glu His Ser Asp Gln Leu Thr Arg Glu Glu Asn Thr Ala		
	2020	2025	2030
	Ile Arg Thr Pro Glu His Leu Ile Ser Gln Lys Gly Phe Ser Tyr Asn		
	2035	2040	2045
	Val Val Asn Ser Ser Ala Phe Ser Gly Phe Ser Thr Ala Ser Gly Lys		
	2050	2055	2060
35	Gln Val Ser Ile Leu Glu Ser Ser Leu His Lys Val Lys Gly Val Leu		
	2065	2070	2075
	Glu Glu Phe Asp Leu Ile Arg Thr Glu His Ser Leu His Tyr Ser Pro		
	2085	2090	2095
40	Thr Ser Arg Gln Asn Val Ser Lys Ile Leu Pro Arg Val Asp Lys Arg		
	2100	2105	2110
	Asn Pro Glu His Cys Val Asn Ser Glu Met Glu Lys Thr Cys Ser Lys		
	2115	2120	2125
	Glu Phe Lys Leu Ser Asn Asn Leu Asn Val Glu Gly Gly Ser Ser Glu		
	2130	2135	2140
45	Asn Asn His Ser Ile Lys Val Ser Pro Tyr Leu Ser Gln Phe Gln Gln		
	2145	2150	2155
	Asp Lys Gln Gln Leu Val Leu Gly Thr Lys Val Ser Leu Val Glu Asn		
	2165	2170	2175
50	Ile His Val Leu Gly Lys Glu Gln Ala Ser Pro Lys Asn Val Lys Met		
	2180	2185	2190
	Glu Ile Gly Lys Thr Glu Thr Phe Ser Asp Val Pro Val Lys Thr Asn		
	2195	2200	2205
	Ile Glu Val Cys Ser Thr Tyr Ser Lys Asp Ser Glu Asn Tyr Phe Glu		
	2210	2215	2220
55	Thr Glu Ala Val Glu Ile Ala Lys Ala Phe Met Glu Asp Asp Glu Leu		
	2225	2230	2235
	Thr Asp Ser Lys Leu Pro Ser His Ala Thr His Ser Leu Phe Thr Cys		
	2245	2250	2255
60	Pro Glu Asn Glu Glu Met Val Leu Ser Asn Ser Arg Ile Gly Lys Arg		
	2260	2265	2270
	Arg Gly Glu Pro Leu Ile Leu Val Gly Glu Pro Ser Ile Lys Arg Asn		
	2275	2280	2285

Leu Leu Asn Glu Phe Asp Arg Ile Ile Glu Asn Gln Glu Lys Ser Leu  
 2290 2295 2300  
 Lys Ala Ser Lys Ser Thr Pro Asp Gly Thr Ile Lys Asp Arg Arg Leu  
 2305 2310 2315 232  
 5 Phe Met His His Val Ser Leu Glu Pro Ile Thr Cys Val Pro Phe Arg  
 2325 2330 2335  
 Thr Thr Lys Glu Arg Gln Glu Ile Gln Asn Pro Asn Phe Thr Ala Pro  
 2340 2345 2350  
 10 Gly Gln Glu Phe Leu Ser Lys Ser His Leu Tyr Glu His Leu Thr Leu  
 2355 2360 2365  
 Glu Lys Ser Ser Ser Asn Leu Ala Val Ser Gly His Pro Phe Tyr Gln  
 2370 2375 2380  
 Val Ser Ala Thr Arg Asn Glu Lys Met Arg His Leu Ile Thr Thr Gly  
 15 2385 2390 2395 240  
 Arg Pro Thr Lys Val Phe Val Pro Pro Phe Lys Thr Lys Ser His Phe  
 2405 2410 2415  
 His Arg Val Glu Gln Cys Val Arg Asn Ile Asn Leu Glu Glu Asn Arg  
 2420 2425 2430  
 20 Gln Lys Gln Asn Ile Asp Gly His Gly Ser Asp Asp Ser Lys Asn Lys  
 2435 2440 2445  
 Ile Asn Asp Asn Glu Ile His Gln Phe Asn Lys Asn Asn Ser Asn Gln  
 2450 2455 2460  
 Ala Ala Ala Val Thr Phe Thr Lys Cys Glu Glu Glu Pro Leu Asp Leu  
 25 2465 2470 2475 248  
 Ile Thr Ser Leu Gln Asn Ala Arg Asp Ile Gln Asp Met Arg Ile Lys  
 2485 2490 2495  
 Lys Lys Gln Arg Gln Arg Val Phe Pro Gln Pro Gly Ser Leu Tyr Leu  
 2500 2505 2510  
 30 Ala Lys Thr Ser Thr Leu Pro Arg Ile Ser Leu Lys Ala Ala Val Gly  
 2515 2520 2525  
 Gly Gln Val Pro Ser Ala Cys Ser His Lys Gln Leu Tyr Thr Tyr Gly  
 2530 2535 2540  
 Val Ser Lys His Cys Ile Lys Ile Asn Ser Lys Asn Ala Glu Ser Phe  
 35 2545 2550 2555 256  
 Gln Phe His Thr Glu Asp Tyr Phe Gly Lys Glu Ser Leu Trp Thr Gly  
 2565 2570 2575  
 Lys Gly Ile Gln Leu Ala Asp Gly Gly Trp Leu Ile Pro Ser Asn Asp  
 2580 2585 2590  
 40 Gly Lys Ala Gly Lys Glu Glu Phe Tyr Arg Ala Leu Cys Asp Thr Pro  
 2595 2600 2605  
 Gly Val Asp Pro Lys Leu Ile Ser Arg Ile Trp Val Tyr Asn His Tyr  
 2610 2615 2620  
 Arg Trp Ile Ile Trp Lys Leu Ala Ala Met Glu Cys Ala Phe Pro Lys  
 45 2625 2630 2635 264  
 Glu Phe Ala Asn Arg Cys Leu Ser Pro Glu Arg Val Leu Leu Gln Leu  
 2645 2650 2655  
 Lys Tyr Arg Tyr Asp Thr Glu Ile Asp Arg Ser Arg Arg Ser Ala Ile  
 2660 2665 2670  
 50 Lys Lys Ile Met Glu Arg Asp Asp Thr Ala Ala Lys Thr Leu Val Leu  
 2675 2680 2685  
 Cys Val Ser Asp Ile Ile Ser Leu Ser Ala Asn Ile Ser Glu Thr Ser  
 2690 2695 2700  
 Ser Asn Lys Thr Ser Ser Ala Asp Thr Gln Lys Val Ala Ile Ile Glu  
 55 2705 2710 2715 272  
 Leu Thr Asp Gly Trp Tyr Ala Val Lys Ala Gln Leu Asp Pro Pro Leu  
 2725 2730 2735  
 Leu Ala Val Leu Lys Asn Gly Arg Leu Thr Val Gly Gln Lys Ile Ile  
 2740 2745 2750  
 60 Leu His Gly Ala Glu Leu Val Gly Ser Pro Asp Ala Cys Thr Pro Leu  
 2755 2760 2765  
 Glu Ala Pro Glu Ser Leu Met Leu Lys Ile Ser Ala Asn Ser Thr Arg

	2770	2775	2780
	Pro Ala Arg Trp Tyr Thr Lys Leu Gly Phe Phe Pro Asp Pro Arg Pro		
	2785	2790	2795 280
5	Phe Pro Leu Pro Leu Ser Ser Leu Phe Ser Asp Gly Gly Asn Val Gly		
	2805	2810	2815
	Cys Val Asp Val Ile Ile Gln Arg Ala Tyr Pro Ile Gln Trp Met Glu		
	2820	2825	2830
10	Lys Thr Ser Ser Gly Leu Tyr Ile Phe Arg Asn Glu Arg Glu Glu Glu		
	2835	2840	2845
	Lys Glu Ala Ala Lys Tyr Val Glu Ala Gln Gln Lys Arg Leu Glu Ala		
	2850	2855	2860
	Leu Phe Thr Lys Ile Gln Glu Glu Phe Glu Glu His Glu Glu Asn Thr		
	2865	2870	2875 288
15	Thr Lys Pro Tyr Leu Pro Ser Arg Ala Leu Thr Arg Gln Gln Val Arg		
	2885	2890	2895
	Ala Leu Gln Asp Gly Ala Glu Leu Tyr Glu Ala Val Lys Asn Ala Ala		
	2900	2905	2910
20	Asp Pro Ala Tyr Leu Glu Gly Tyr Phe Ser Glu Glu Gln Leu Arg Ala		
	2915	2920	2925
	Leu Asn Asn His Arg Gln Met Leu Asn Asp Lys Lys Gln Ala Gln Ile		
	2930	2935	2940
	Gln Leu Glu Ile Arg Lys Ala Met Glu Ser Ala Glu Gln Lys Glu Gln		
	2945	2950	2955 296
25	Gly Leu Ser Arg Asp Val Thr Thr Val Trp Lys Leu Arg Ile Val Ser		
	2965	2970	2975
	Tyr Ser Lys Lys Glu Lys Asp Ser Val Ile Leu Ser Ile Trp Arg Pro		
	2980	2985	2990
30	Ser Ser Asp Leu Tyr Ser Leu Leu Thr Glu Gly Lys Arg Tyr Arg Ile		
	2995	3000	3005
	Tyr His Leu Ala Thr Ser Lys Ser Lys Ser Lys Ser Glu Arg Ala Asn		
	3010	3015	3020
	Ile Gln Leu Ala Ala Thr Lys Lys Thr Gln Tyr Gln Gln Leu Pro Val		
	3025	3030	3035 304
35	Ser Asp Glu Ile Leu Phe Gln Ile Tyr Gln Pro Arg Glu Pro Leu His		
	3045	3050	3055
	Phe Ser Lys Phe Leu Asp Pro Asp Phe Gln Pro Ser Cys Ser Glu Val		
	3060	3065	3070
40	Asp Leu Ile Gly Phe Val Val Ser Val Val Lys Lys Thr Gly Leu Ala		
	3075	3080	3085
	Pro Phe Val Tyr Leu Ser Asp Glu Cys Tyr Asn Leu Leu Ala Ile Lys		
	3090	3095	3100
	Phe Trp Ile Asp Leu Asn Glu Asp Ile Ile Lys Pro His Met Leu Ile		
	3105	3110	3115 312
45	Ala Ala Ser Asn Leu Gln Trp Arg Pro Glu Ser Lys Ser Gly Leu Leu		
	3125	3130	3135
	Thr Leu Phe Ala Gly Asp Phe Ser Val Phe Ser Ala Ser Pro Lys Glu		
	3140	3145	3150
50	Gly His Phe Gln Glu Thr Phe Asn Lys Met Lys Asn Thr Val Glu Asn		
	3155	3160	3165
	Ile Asp Ile Leu Cys Asn Glu Ala Glu Asn Lys Leu Met His Ile Leu		
	3170	3175	3180
	His Ala Asn Asp Pro Lys Trp Ser Thr Pro Thr Lys Asp Cys Thr Ser		
	3185	3190	3195 320
55	Gly Pro Tyr Thr Ala Gln Ile Ile Pro Gly Thr Gly Asn Lys Leu Leu		
	3205	3210	3215
	Met Ser Ser Pro Asn Cys Glu Ile Tyr Tyr Gln Ser Pro Leu Ser Leu		
	3220	3225	3230
60	Cys Met Ala Lys Arg Lys Ser Val Ser Thr Pro Val Ser Ala Gln Met		
	3235	3240	3245
	Thr Ser Lys Ser Cys Lys Gly Glu Lys Glu Ile Asp Asp Gln Lys Asn		
	3250	3255	3260

Cys Lys Lys Arg Arg Ala Leu Asp Phe Leu Ser Arg Leu Pro Leu Pro  
 3265 3270 3275 328  
 Pro Pro Val Ser Pro Ile Cys Thr Phe Val Ser Pro Ala Ala Gln Lys  
 3285 3290 3295  
 5 Ala Phe Gln Pro Pro Arg Ser Cys Gly Thr Lys Tyr Glu Thr Pro Ile  
 3300 3305 3310  
 Lys Lys Lys Glu Leu Asn Ser Pro Gln Met Thr Pro Phe Lys Lys Phe  
 3315 3320 3325  
 10 Asn Glu Ile Ser Leu Leu Glu Ser Asn Ser Ile Ala Asp Glu Glu Leu  
 3330 3335 3340  
 Ala Leu Ile Asn Thr Gln Ala Leu Leu Ser Gly Ser Thr Gly Glu Lys  
 3345 3350 3355 336  
 Gln Phe Ile Ser Val Ser Glu Ser Thr Arg Thr Ala Pro Thr Ser Ser  
 3365 3370 3375  
 15 Glu Asp Tyr Leu Arg Leu Lys Arg Arg Cys Thr Thr Ser Leu Ile Lys  
 3380 3385 3390  
 Glu Gln Glu Ser Ser Gln Ala Ser Thr Glu Glu Cys Glu Lys Asn Lys  
 3395 3400 3405  
 20 Gln Asp Thr Ile Thr Thr Lys Lys Tyr Ile  
 3410 3415

## (2) INFORMATION FOR SEQ ID NO:8:

- 25 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 10485 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear  
 30 (ii) MOLECULE TYPE: cDNA  
 (ix) FEATURE:  
 (A) NAME/KEY: Coding Sequence  
 35 (B) LOCATION: 229...10482  
 (D) OTHER INFORMATION: BRCA2 (OMI3)

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

40 GGTGGCGCGA GCTTCTGAAA CTAGGCGGCA GAGGCGGAGC CGCTGTGGCA CTGCTGCGCC 60  
 TCTGCTGCGC CTCGGGTGTC TTTTGCGGCG GTGGGTCGCC GCCGGGAGAA GCGTGAGGGG 120  
 ACAGATTGTG GACCGGCGCG GTTTTGTCA GCTTACTCCG GCCAAAAAAG AACTGCACCT 180  
 CTGGAGCGGA CTTATTTACC AAGCATTGGA GGAATATCGT AGGTAAAA ATG CCT ATT 237  
 Met Pro Ile  
 45 1  
 GGA TCC AAA GAG AGG CCA ACA TTT TTT GAA ATT TTT AAG ACA CGC TGC 285  
 Gly Ser Lys Glu Arg Pro Thr Phe Phe Glu Ile Phe Lys Thr Arg Cys  
 5 10 15  
 50 AAC AAA GCA GAT TTA GGA CCA ATA AGT CTT AAT TGG TTT GAA GAA CTT 333  
 Asn Lys Ala Asp Leu Gly Pro Ile Ser Leu Asn Trp Phe Glu Glu Leu  
 20 25 30 35  
 55 TCT TCA GAA GCT CCA CCC TAT AAT TCT GAA CCT GCA GAA GAA TCT GAA 381  
 Ser Ser Glu Ala Pro Pro Tyr Asn Ser Glu Pro Ala Glu Glu Ser Glu  
 40 45 50  
 60 CAT AAA AAC AAC AAT TAC GAA CCA AAC CTA TTT AAA ACT CCA CAA AGG 429  
 His Lys Asn Asn Asn Tyr Glu Pro Asn Leu Phe Lys Thr Pro Gln Arg  
 55 60 65

	AAA	CCA	TCT	TAT	AAT	CAG	CTG	GCT	TCA	ACT	CCA	ATA	ATA	TTC	AAA	GAG	477
	Lys	Pro	Ser	Tyr	Asn	Gln	Leu	Ala	Ser	Thr	Pro	Ile	Ile	Phe	Lys	Glu	
			70					75						80			
5	CAA	GGG	CTG	ACT	CTG	CCG	CTG	TAC	CAA	TCT	CCT	GTA	AAA	GAA	TTA	GAT	525
	Gln	Gly	Leu	Thr	Leu	Pro	Leu	Tyr	Gln	Ser	Pro	Val	Lys	Glu	Leu	Asp	
		85					90					95					
10	AAA	TTC	AAA	TTA	GAC	TTA	GGA	AGG	AAT	GTT	CCC	AAT	AGT	AGA	CAT	AAA	573
	Lys	Phe	Lys	Leu	Asp	Leu	Gly	Arg	Asn	Val	Pro	Asn	Ser	Arg	His	Lys	
	100					105					110					115	
15	AGT	CTT	CGC	ACA	GTG	AAA	ACT	AAA	ATG	GAT	CAA	GCA	GAT	GAT	GTT	TCC	621
	Ser	Leu	Arg	Thr	Val	Lys	Thr	Lys	Met	Asp	Gln	Ala	Asp	Asp	Val	Ser	
				120						125					130		
20	TGT	CCA	CTT	CTA	AAT	TCT	TGT	CTT	AGT	GAA	AGT	CCT	GTT	GTT	CTA	CAA	669
	Cys	Pro	Leu	Leu	Asn	Ser	Cys	Leu	Ser	Glu	Ser	Pro	Val	Val	Leu	Gln	
				135					140					145			
25	TGT	ACA	CAT	GTA	ACA	CCA	CAA	AGA	GAT	AAG	TCA	GTG	GTA	TGT	GGG	AGT	717
	Cys	Thr	His	Val	Thr	Pro	Gln	Arg	Asp	Lys	Ser	Val	Val	Cys	Gly	Ser	
		150						155					160				
30	TTG	TTT	CAT	ACA	CCA	AAG	TTT	GTG	AAG	GGT	CGT	CAG	ACA	CCA	AAA	CAT	765
	Leu	Phe	His	Thr	Pro	Lys	Phe	Val	Lys	Gly	Arg	Gln	Thr	Pro	Lys	His	
		165					170					175					
35	ATT	TCT	GAA	AGT	CTA	GGA	GCT	GAG	GTG	GAT	CCT	GAT	ATG	TCT	TGG	TCA	813
	Ile	Ser	Glu	Ser	Leu	Gly	Ala	Glu	Val	Asp	Pro	Asp	Met	Ser	Trp	Ser	
	180					185					190					195	
40	AGT	TCT	TTA	GCT	ACA	CCA	CCC	ACC	CTT	AGT	TCT	ACT	GTG	CTC	ATA	GTC	861
	Ser	Ser	Leu	Ala	Thr	Pro	Pro	Thr	Leu	Ser	Ser	Thr	Val	Leu	Ile	Val	
				200						205					210		
45	AGA	AAT	GAA	GAA	GCA	TCT	GAA	ACT	GTA	TTT	CCT	CAT	GAT	ACT	ACT	GCT	909
	Arg	Asn	Glu	Glu	Ala	Ser	Glu	Thr	Val	Phe	Pro	His	Asp	Thr	Thr	Ala	
				215					220					225			
50	AAT	GTG	AAA	AGC	TAT	TTT	TCC	AAT	CAT	GAT	GAA	AGT	CTG	AAG	AAA	AAT	957
	Asn	Val	Lys	Ser	Tyr	Phe	Ser	Asn	His	Asp	Glu	Ser	Leu	Lys	Lys	Asn	
		230					235						240				
55	GAT	AGA	TTT	ATC	GCT	TCT	GTG	ACA	GAC	AGT	GAA	AAC	ACA	AAT	CAA	AGA	1005
	Asp	Arg	Phe	Ile	Ala	Ser	Val	Thr	Asp	Ser	Glu	Asn	Thr	Asn	Gln	Arg	
		245					250					255					
60	GAA	GCT	GCA	AGT	CAT	GGA	TTT	GGA	AAA	ACA	TCA	GGG	AAT	TCA	TTT	AAA	1053
	Glu	Ala	Ala	Ser	His	Gly	Phe	Gly	Lys	Thr	Ser	Gly	Asn	Ser	Phe	Lys	
	260					265					270					275	
65	GTA	AAT	AGC	TGC	AAA	GAC	CAC	ATT	GGA	AAG	TCA	ATG	CCA	CAT	GTC	CTA	1101
	Val	Asn	Ser	Cys	Lys	Asp	His	Ile	Gly	Lys	Ser	Met	Pro	His	Val	Leu	
				280						285					290		
70	GAA	GAT	GAA	GTA	TAT	GAA	ACA	GTT	GTA	GAT	ACC	TCT	GAA	GAA	GAT	AGT	1149
	Glu	Asp	Glu	Val	Tyr	Glu	Thr	Val	Val	Asp	Thr	Ser	Glu	Glu	Asp	Ser	
				295					300					305			
75	TTT	TCA	TTA	TGT	TTT	TCT	AAA	TGT	AGA	ACA	AAA	AAT	CTA	CAA	AAA	GTA	1197



	Phe	Ser	Leu	Cys	Phe	Ser	Lys	Cys	Arg	Thr	Lys	Asn	Leu	Gln	Lys	Val	
			310					315					320				
5	AGA	ACT	AGC	AAG	ACT	AGG	AAA	AAA	ATT	TTC	CAT	GAA	GCA	AAC	GCT	GAT	1245
	Arg	Thr	Ser	Lys	Thr	Arg	Lys	Lys	Ile	Phe	His	Glu	Ala	Asn	Ala	Asp	
			325					330					335				
10	GAA	TGT	GAA	AAA	TCT	AAA	AAC	CAA	GTG	AAA	GAA	AAA	TAC	TCA	TTT	GTA	1293
	Glu	Cys	Glu	Lys	Ser	Lys	Asn	Gln	Val	Lys	Glu	Lys	Tyr	Ser	Phe	Val	
			340					345					350			355	
15	TCT	GAA	GTG	GAA	CCA	AAT	GAT	ACT	GAT	CCA	TTA	GAT	TCA	AAT	GTA	GCA	1341
	Ser	Glu	Val	Glu	Pro	Asn	Asp	Thr	Asp	Pro	Leu	Asp	Ser	Asn	Val	Ala	
					360					365					370		
20	AAT	CAG	AAG	CCC	TTT	GAG	AGT	GGA	AGT	GAC	AAA	ATC	TCC	AAG	GAA	GTT	1389
	Asn	Gln	Lys	Pro	Phe	Glu	Ser	Gly	Ser	Asp	Lys	Ile	Ser	Lys	Glu	Val	
				375					380					385			
25	GTA	CCG	TCT	TTG	GCC	TGT	GAA	TGG	TCT	CAA	CTA	ACC	CTT	TCA	GGT	CTA	1437
	Val	Pro	Ser	Leu	Ala	Cys	Glu	Trp	Ser	Gln	Leu	Thr	Leu	Ser	Gly	Leu	
				390					395					400			
30	AAT	GGA	GCC	CAG	ATG	GAG	AAA	ATA	CCC	CTA	TTG	CAT	ATT	TCT	TCA	TGT	1485
	Asn	Gly	Ala	Gln	Met	Glu	Lys	Ile	Pro	Leu	Leu	His	Ile	Ser	Ser	Cys	
								410					415				
35	GAC	CAA	AAT	ATT	TCA	GAA	AAA	GAC	CTA	TTA	GAC	ACA	GAG	AAC	AAA	AGA	1533
	Asp	Gln	Asn	Ile	Ser	Glu	Lys	Asp	Leu	Leu	Asp	Thr	Glu	Asn	Lys	Arg	
								425				430				435	
40	AAG	AAA	GAT	TTT	CTT	ACT	TCA	GAG	AAT	TCT	TTG	CCA	CGT	ATT	TCT	AGC	1581
	Lys	Lys	Asp	Phe	Leu	Thr	Ser	Glu	Asn	Ser	Leu	Pro	Arg	Ile	Ser	Ser	
								440				445				450	
45	CTA	CCA	AAA	TCA	GAG	AAG	CCA	TTA	AAT	GAG	GAA	ACA	GTG	GTA	AAT	AAG	1629
	Leu	Pro	Lys	Ser	Glu	Lys	Pro	Leu	Asn	Glu	Glu	Thr	Val	Val	Asn	Lys	
								455						465			
50	AGA	GAT	GAA	GAG	CAG	CAT	CTT	GAA	TCT	CAT	ACA	GAC	TGC	ATT	CTT	GCA	1677
	Arg	Asp	Glu	Glu	Gln	His	Leu	Glu	Ser	His	Thr	Asp	Cys	Ile	Leu	Ala	
								475					480				
55	GTA	AAG	CAG	GCA	ATA	TCT	GGA	ACT	TCT	CCA	GTG	GCT	TCT	TCA	TTT	CAG	1725
	Val	Lys	Gln	Ala	Ile	Ser	Gly	Thr	Ser	Pro	Val	Ala	Ser	Ser	Phe	Gln	
								490					495				
60	GGT	ATC	AAA	AAG	TCT	ATA	TTC	AGA	ATA	AGA	GAA	TCA	CCT	AAA	GAG	ACT	1773
	Gly	Ile	Lys	Lys	Ser	Ile	Phe	Arg	Ile	Arg	Glu	Ser	Pro	Lys	Glu	Thr	
								505				510				515	
65	TTC	AAT	GCA	AGT	TTT	TCA	GGT	CAT	ATG	ACT	GAT	CCA	AAC	TTT	AAA	AAA	1821
	Phe	Asn	Ala	Ser	Phe	Ser	Gly	His	Met	Thr	Asp	Pro	Asn	Phe	Lys	Lys	
								520				525				530	
70	GAA	ACT	GAA	GCC	TCT	GAA	AGT	GGA	CTG	GAA	ATA	CAT	ACT	GTT	TGC	TCA	1869
	Glu	Thr	Glu	Ala	Ser	Glu	Ser	Gly	Leu	Glu	Ile	His	Thr	Val	Cys	Ser	
								535						545			
75	CAG	AAG	GAG	GAC	TCC	TTA	TGT	CCA	AAT	TTA	ATT	GAT	AAT	GGA	AGC	TGG	1917
	Gln	Lys	Glu	Asp	Ser	Leu	Cys	Pro	Asn	Leu	Ile	Asp	Asn	Gly	Ser	Trp	

	550	555	560	
5	CCA GCC ACC ACC ACA CAG AAT TCT GTA GCT TTG AAG AAT GCA GGT TTA Pro Ala Thr Thr Thr Gln Asn Ser Val Ala Leu Lys Asn Ala Gly Leu 565 570 575	1965		
10	ATA TCC ACT TTG AAA AAG AAA ACA AAT AAG TTT ATT TAT GCT ATA CAT Ile Ser Thr Leu Lys Lys Lys Thr Asn Lys Phe Ile Tyr Ala Ile His 580 585 590 595	2013		
15	GAT GAA ACA TCT TAT AAA GGA AAA AAA ATA CCG AAA GAC CAA AAA TCA Asp Glu Thr Ser Tyr Lys Gly Lys Lys Ile Pro Lys Asp Gln Lys Ser 600 605 610	2061		
20	GAA CTA ATT AAC TGT TCA GCC CAG TTT GAA GCA AAT GCT TTT GAA GCA Glu Leu Ile Asn Cys Ser Ala Gln Phe Glu Ala Asn Ala Phe Glu Ala 615 620 625	2109		
25	CCA CTT ACA TTT GCA AAT GCT GAT TCA GGT TTA TTG CAT TCT TCT GTG Pro Leu Thr Phe Ala Asn Ala Asp Ser Gly Leu Leu His Ser Ser Val 630 635 640	2157		
30	AAA AGA AGC TGT TCA CAG AAT GAT TCT GAA GAA CCA ACT TTG TCC TTA Lys Arg Ser Cys Ser Gln Asn Asp Ser Glu Glu Pro Thr Leu Ser Leu 645 650 655	2205		
35	ACT AGC TCT TTT GGG ACA ATT CTG AGG AAA TGT TCT AGA AAT GAA ACA Thr Ser Ser Phe Gly Thr Ile Leu Arg Lys Cys Ser Arg Asn Glu Thr 660 665 670 675	2253		
40	TGT TCT AAT AAT ACA GTA ATC TCT CAG GAT CTT GAT TAT AAA GAA GCA Cys Ser Asn Asn Thr Val Ile Ser Gln Asp Leu Asp Tyr Lys Glu Ala 680 685 690	2301		
45	AAA TGT AAT AAG GAA AAA CTA CAG TTA TTT ATT ACC CCA GAA GCT GAT Lys Cys Asn Lys Glu Lys Leu Gln Leu Phe Ile Thr Pro Glu Ala Asp 695 700 705	2349		
50	TCT CTG TCA TGC CTG CAG GAA GGA CAG TGT GAA AAT GAT CCA AAA AGC Ser Leu Ser Cys Leu Gln Glu Gly Gln Cys Glu Asn Asp Pro Lys Ser 710 715 720	2397		
55	AAA AAA GTT TCA GAT ATA AAA GAA GAG GTC TTG GCT GCA GCA TGT CAC Lys Lys Val Ser Asp Ile Lys Glu Glu Val Leu Ala Ala Ala Cys His 725 730 735	2445		
60	CCA GTA CAA CAC TCA AAA GTG GAA TAC AGT GAT ACT GAC TTT CAA TCC Pro Val Gln His Ser Lys Val Glu Tyr Ser Asp Thr Asp Phe Gln Ser 740 745 750 755	2493		
65	CAG AAA AGT CTT TTA TAT GAT CAT GAA AAT GCC AGC ACT CTT ATT TTA Gln Lys Ser Leu Leu Tyr Asp His Glu Asn Ala Ser Thr Leu Ile Leu 760 765 770	2541		
70	ACT CCT ACT TCC AAG GAT GTT CTG TCA AAC CTA GTC ATG ATT TCT AGA Thr Pro Thr Ser Lys Asp Val Leu Ser Asn Leu Val Met Ile Ser Arg 775 780 785	2589		
75	GGC AAA GAA TCA TAC AAA ATG TCA GAC AAG CTC AAA GGT AAC AAT TAT Gly Lys Glu Ser Tyr Lys Met Ser Asp Lys Leu Lys Gly Asn Asn Tyr 790 795 800	2637		

5	GAA TCT GAT GTT GAA TTA ACC AAA AAT ATT CCC ATG GAA AAG AAT CAA Glu Ser Asp Val Glu Leu Thr Lys Asn Ile Pro Met Glu Lys Asn Gln 805 810 815	2685
10	GAT GTA TGT GCT TTA AAT GAA AAT TAT AAA AAC GTT GAG CTG TTG CCA Asp Val Cys Ala Leu Asn Glu Asn Tyr Lys Asn Val Glu Leu Leu Pro 820 825 830 835	2733
15	CCT GAA AAA TAC ATG AGA GTA GCA TCA CCT TCA AGA AAG GTA CAA TTC Pro Glu Lys Tyr Met Arg Val Ala Ser Pro Ser Arg Lys Val Gln Phe 840 845 850	2781
20	AAC CAA AAC ACA AAT CTA AGA GTA ATC CAA AAA AAT CAA GAA GAA ACT Asn Gln Asn Thr Asn Leu Arg Val Ile Gln Lys Asn Gln Glu Glu Thr 855 860 865	2829
25	ACT TCA ATT TCA AAA ATA ACT GTC AAT CCA GAC TCT GAA GAA CTT TTC Thr Ser Ile Ser Lys Ile Thr Val Asn Pro Asp Ser Glu Glu Leu Phe 870 875 880	2877
30	TCA GAC AAT GAG AAT AAT TTT GTC TTC CAA GTA GCT AAT GAA AGG AAT Ser Asp Asn Glu Asn Asn Phe Val Phe Gln Val Ala Asn Glu Arg Asn 885 890 895	2925
35	AAT CTT GCT TTA GGA AAT ACT AAG GAA CTT CAT GAA ACA GAC TTG ACT Asn Leu Ala Leu Gly Asn Thr Lys Glu Leu His Glu Thr Asp Leu Thr 900 905 910 915	2973
40	TGT GTA AAC GAA CCC ATT TTC AAG AAC TCT ACC ATG GTT TTA TAT GGA Cys Val Asn Glu Pro Ile Phe Lys Asn Ser Thr Met Val Leu Tyr Gly 920 925 930	3021
45	GAC ACA GGT GAT AAA CAA GCA ACC CAA GTG TCA ATT AAA AAA GAT TTG Asp Thr Gly Asp Lys Gln Ala Thr Gln Val Ser Ile Lys Lys Asp Leu 935 940 945	3069
50	GTT TAT GTT CTT GCA GAG GAG AAC AAA AAT AGT GTA AAG CAG CAT ATA Val Tyr Val Leu Ala Glu Glu Asn Lys Asn Ser Val Lys Gln His Ile 950 955 960	3117
55	AAA ATG ACT CTA GGT CAA GAT TTA AAA TCG GAC ATC TCC TTG AAT ATA Lys Met Thr Leu Gly Gln Asp Leu Lys Ser Asp Ile Ser Leu Asn Ile 965 970 975	3165
60	GAT AAA ATA CCA GAA AAA AAT AAT GAT TAC ATG GAC AAA TGG GCA GGA Asp Lys Ile Pro Glu Lys Asn Asn Asp Tyr Met Asp Lys Trp Ala Gly 980 985 990 995	3213
65	CTC TTA GGT CCA ATT TCA AAT CAC AGT TTT GGA GGT AGC TTC AGA ACA Leu Leu Gly Pro Ile Ser Asn His Ser Phe Gly Gly Ser Phe Arg Thr 1000 1005 1010	3261
70	GCT TCA AAT AAG GAA ATC AAG CTC TCT GAA CAT AAC ATT AAG AAG AGC Ala Ser Asn Lys Glu Ile Lys Leu Ser Glu His Asn Ile Lys Lys Ser 1015 1020 1025	3309
75	AAA ATG TTC TTC AAA GAT ATT GAA GAA CAA TAT CCT ACT AGT TTA GCT Lys Met Phe Phe Lys Asp Ile Glu Glu Gln Tyr Pro Thr Ser Leu Ala 1030 1035 1040	3357

	TGT GTT GAA ATT GTA AAT ACC TTG GCA TTA GAT AAT CAA AAG AAA CTG	3405
	Cys Val Glu Ile Val Asn Thr Leu Ala Leu Asp Asn Gln Lys Lys Leu	
	1045 1050 1055	
5	AGC AAG CCT CAG TCA ATT AAT ACT GTA TCT GCA CAT TTA CAG AGT AGT	3453
	Ser Lys Pro Gln Ser Ile Asn Thr Val Ser Ala His Leu Gln Ser Ser	
	1060 1065 1070 1075	
10	GTA GTT GTT TCT GAT TGT AAA AAT AGT CAT ATA ACC CCT CAG ATG TTA	3501
	Val Val Val Ser Asp Cys Lys Asn Ser His Ile Thr Pro Gln Met Leu	
	1080 1085 1090	
15	TTT TCC AAG CAG GAT TTT AAT TCA AAC CAT AAT TTA ACA CCT AGC CAA	3549
	Phe Ser Lys Gln Asp Phe Asn Ser Asn His Asn Leu Thr Pro Ser Gln	
	1095 1100 1105	
20	AAG GCA GAA ATT ACA GAA CTT TCT ACT ATA TTA GAA GAA TCA GGA AGT	3597
	Lys Ala Glu Ile Thr Glu Leu Ser Thr Ile Leu Glu Glu Ser Gly Ser	
	1110 1115 1120	
25	CAG TTT GAA TTT ACT CAG TTT AGA AAG CCA AGC TAC ATA TTG CAG AAG	3645
	Gln Phe Glu Phe Thr Gln Phe Arg Lys Pro Ser Tyr Ile Leu Gln Lys	
	1125 1130 1135	
30	AGT ACA TTT GAA GTG CCT GAA AAC CAG ATG ACT ATC TTA AAG ACC ACT	3693
	Ser Thr Phe Glu Val Pro Glu Asn Gln Met Thr Ile Leu Lys Thr Thr	
	1140 1145 1150 1155	
35	TCT GAG GAA TGC AGA GAT GCT GAT CTT CAT GTC ATA ATG AAT GCC CCA	3741
	Ser Glu Glu Cys Arg Asp Ala Asp Leu His Val Ile Met Asn Ala Pro	
	1160 1165 1170	
40	TCG ATT GGT CAG GTA GAC AGC AGC AAG CAA TTT GAA GGT ACA GTT GAA	3789
	Ser Ile Gly Gln Val Asp Ser Ser Lys Gln Phe Glu Gly Thr Val Glu	
	1175 1180 1185	
45	ATT AAA CGG AAG TTT GCT GGC CTG TTG AAA AAT GAC TGT AAC AAA AGT	3837
	Ile Lys Arg Lys Phe Ala Gly Leu Leu Lys Asn Asp Cys Asn Lys Ser	
	1190 1195 1200	
50	GCT TCT GGT TAT TTA ACA GAT GAA AAT GAA GTG GGG TTT AGG GGC TTT	3885
	Ala Ser Gly Tyr Leu Thr Asp Glu Asn Glu Val Gly Phe Arg Gly Phe	
	1205 1210 1215	
55	TAT TCT GCT CAT GGC ACA AAA CTG AAT GTT TCT ACT GAA GCT CTG CAA	3933
	Tyr Ser Ala His Gly Thr Lys Leu Asn Val Ser Thr Glu Ala Leu Gln	
	1220 1225 1230 1235	
60	AAA GCT GTG AAA CTG TTT AGT GAT ATT GAG AAT ATT AGT GAG GAA ACT	3981
	Lys Ala Val Lys Leu Phe Ser Asp Ile Glu Asn Ile Ser Glu Glu Thr	
	1240 1245 1250	
65	TCT GCA GAG GTA CAT CCA ATA AGT TTA TCT TCA AGT AAA TGT CAT GAT	4029
	Ser Ala Glu Val His Pro Ile Ser Leu Ser Ser Ser Lys Cys His Asp	
	1255 1260 1265	
70	TCT GTT GTT TCA ATG TTT AAG ATA GAA AAT CAT AAT GAT AAA ACT GTA	4077
	Ser Val Val Ser Met Phe Lys Ile Glu Asn His Asn Asp Lys Thr Val	
	1270 1275 1280	
75	AGT GAA AAA AAT AAT AAT TGC CAA CTG ATA TTA CAA AAT AAT ATT GAA	4125

	Ser	Glu	Lys	Asn	Asn	Lys	Cys	Gln	Leu	Ile	Leu	Gln	Asn	Asn	Ile	Glu	
	1285						1290					1295					
5	ATG	ACT	ACT	GGC	ACT	TTT	GTT	GAA	GAA	ATT	ACT	GAA	AAT	TAC	AAG	AGA	4173
	Met	Thr	Thr	Gly	Thr	Phe	Val	Glu	Glu	Ile	Thr	Glu	Asn	Tyr	Lys	Arg	
	1300					1305					1310					1315	
10	AAT	ACT	GAA	AAT	GAA	GAT	AAC	AAA	TAT	ACT	GCT	GCC	AGT	AGA	AAT	TCT	4221
	Asn	Thr	Glu	Asn	Glu	Asp	Asn	Lys	Tyr	Thr	Ala	Ala	Ser	Arg	Asn	Ser	
					1320					1325						1330	
15	CAT	AAC	TTA	GAA	TTT	GAT	GGC	AGT	GAT	TCA	AGT	AAA	AAT	GAT	ACT	GTT	4269
	His	Asn	Leu	Glu	Phe	Asp	Gly	Ser	Asp	Ser	Ser	Lys	Asn	Asp	Thr	Val	
				1335					1340						1345		
20	TGT	ATT	CAT	AAA	GAT	GAA	ACG	GAC	TTG	CTA	TTT	ACT	GAT	CAG	CAC	AAC	4317
	Cys	Ile	His	Lys	Asp	Glu	Thr	Asp	Leu	Leu	Phe	Thr	Asp	Gln	His	Asn	
		1350						1355						1360			
25	ATA	TGT	CTT	AAA	TTA	TCT	GGC	CAG	TTT	ATG	AAG	GAG	GGA	AAC	ACT	CAG	4365
	Ile	Cys	Leu	Lys	Leu	Ser	Gly	Gln	Phe	Met	Lys	Glu	Gly	Asn	Thr	Gln	
		1365					1370						1375				
30	ATT	AAA	GAA	GAT	TTG	TCA	GAT	TTA	ACT	TTT	TTG	GAA	GTT	GCG	AAA	GCT	4413
	Ile	Lys	Glu	Asp	Leu	Ser	Asp	Leu	Thr	Phe	Leu	Glu	Val	Ala	Lys	Ala	
	1380					1385					1390					1395	
35	CAA	GAA	GCA	TGT	CAT	GGT	AAT	ACT	TCA	AAT	AAA	GAA	CAG	TTA	ACT	GCT	4461
	Gln	Glu	Ala	Cys	His	Gly	Asn	Thr	Ser	Asn	Lys	Glu	Gln	Leu	Thr	Ala	
					1400					1405						1410	
40	ACT	AAA	ACG	GAG	CAA	AAT	ATA	AAA	GAT	TTT	GAG	ACT	TCT	GAT	ACA	TTT	4509
	Thr	Lys	Thr	Glu	Gln	Asn	Ile	Lys	Asp	Phe	Glu	Thr	Ser	Asp	Thr	Phe	
				1415					1420						1425		
45	TTT	CAG	ACT	GCA	AGT	GGG	AAA	AAT	ATT	AGT	GTC	GCC	AAA	GAG	TCA	TTT	4557
	Phe	Gln	Thr	Ala	Ser	Gly	Lys	Asn	Ile	Ser	Val	Ala	Lys	Glu	Ser	Phe	
		1430						1435						1440			
50	AAT	AAA	ATT	GTA	AAT	TTC	TTT	GAT	CAG	AAA	CCA	GAA	GAA	TTG	CAT	AAC	4605
	Asn	Lys	Ile	Val	Asn	Phe	Phe	Asp	Gln	Lys	Pro	Glu	Glu	Leu	His	Asn	
		1445					1450						1455				
55	TTT	TCC	TTA	AAT	TCT	GAA	TTA	CAT	TCT	GAC	ATA	AGA	AAG	AAC	AAA	ATG	4653
	Phe	Ser	Leu	Asn	Ser	Glu	Leu	His	Ser	Asp	Ile	Arg	Lys	Asn	Lys	Met	
	1460					1465					1470					1475	
60	GAC	ATT	CTA	AGT	TAT	GAG	GAA	ACA	GAC	ATA	GTT	AAA	CAC	AAA	ATA	CTG	4701
	Asp	Ile	Leu	Ser	Tyr	Glu	Glu	Thr	Asp	Ile	Val	Lys	His	Lys	Ile	Leu	
					1480					1485					1490		
65	AAA	GAA	AGT	GTC	CCA	GTT	GGT	ACT	GGA	AAT	CAA	CTA	GTG	ACC	TTC	CAG	4749
	Lys	Glu	Ser	Val	Pro	Val	Gly	Thr	Gly	Asn	Gln	Leu	Val	Thr	Phe	Gln	
				1495					1500						1505		
70	GGA	CAA	CCC	GAA	CGT	GAT	GAA	AAG	ATC	AAA	GAA	CCT	ACT	CTG	TTG	GGT	4797
	Gly	Gln	Pro	Glu	Arg	Asp	Glu	Lys	Ile	Lys	Glu	Pro	Thr	Leu	Leu	Gly	
		1510						1515						1520			
75	TTT	CAT	ACA	GCT	AGC	GGG	AAA	AAA	GTT	AAA	ATT	GCA	AAG	GAA	TCT	TTG	4845
	Phe	His	Thr	Ala	Ser	Gly	Lys	Lys	Val	Lys	Ile	Ala	Lys	Glu	Ser	Leu	

	1525	1530	1535	
5	GAC AAA GTG AAA AAC CTT TTT GAT GAA AAA GAG CAA GGT ACT AGT GAA Asp Lys Val Lys Asn Leu Phe Asp Glu Lys Glu Gln Gly Thr Ser Glu 1540 1545 1550 1555	4893		
10	ATC ACC AGT TTT AGC CAT CAA TGG GCA AAG ACC CTA AAG TAC AGA GAG Ile Thr Ser Phe Ser His Gln Trp Ala Lys Thr Leu Lys Tyr Arg Glu 1560 1565 1570	4941		
15	GCC TGT AAA GAC CTT GAA TTA GCA TGT GAG ACC ATT GAG ATC ACA GCT Ala Cys Lys Asp Leu Glu Leu Ala Cys Glu Thr Ile Glu Ile Thr Ala 1575 1580 1585	4989		
20	GCC CCA AAG TGT AAA GAA ATG CAG AAT TCT CTC AAT AAT GAT AAA AAC Ala Pro Lys Cys Lys Glu Met Gln Asn Ser Leu Asn Asn Asp Lys Asn 1590 1595 1600	5037		
25	CTT GTT TCT ATT GAG ACT GTG GTG CCA CCT AAG CTC TTA AGT GAT AAT Leu Val Ser Ile Glu Thr Val Val Pro Pro Lys Leu Leu Ser Asp Asn 1605 1610 1615	5085		
30	TTA TGT AGA CAA ACT GAA AAT CTC AAA ACA TCA AAA AGT ATC TTT TTG Leu Cys Arg Gln Thr Glu Asn Leu Lys Thr Ser Lys Ser Ile Phe Leu 1620 1625 1630 1635	5133		
35	AAA GTT AAA GTA CAT GAA AAT GTA GAA AAA GAA ACA GCA AAA AGT CCT Lys Val Lys Val His Glu Asn Val Glu Lys Glu Thr Ala Lys Ser Pro 1640 1645 1650	5181		
40	GCA ACT TGT TAC ACA AAT CAG TCC CCT TAT TCA GTC ATT GAA AAT TCA Ala Thr Cys Tyr Thr Asn Gln Ser Pro Tyr Ser Val Ile Glu Asn Ser 1655 1660 1665	5229		
45	GCC TTA GCT TTT TAC ACA AGT TGT AGT AGA AAA ACT TCT GTG AGT CAG Ala Leu Ala Phe Tyr Thr Ser Cys Ser Arg Lys Thr Ser Val Ser Gln 1670 1675 1680	5277		
50	ACT TCA TTA CTT GAA GCA AAA AAA TGG CTT AGA GAA GGA ATA TTT GAT Thr Ser Leu Leu Glu Ala Lys Lys Trp Leu Arg Glu Gly Ile Phe Asp 1685 1690 1695	5325		
55	GGT CAA CCA GAA AGA ATA AAT ACT GCA GAT TAT GTA GGA AAT TAT TTG Gly Gln Pro Glu Arg Ile Asn Thr Ala Asp Tyr Val Gly Asn Tyr Leu 1700 1705 1710 1715	5373		
60	TAT GAA AAT AAT TCA AAC AGT ACT ATA GCT GAA AAT GAC AAA AAT CAT Tyr Glu Asn Asn Ser Asn Ser Thr Ile Ala Glu Asn Asp Lys Asn His 1720 1725 1730	5421		
65	CTC TCC GAA AAA CAA GAT ACT TAT TTA AGT AAC AGT AGC ATG TCT AAC Leu Ser Glu Lys Gln Asp Thr Tyr Leu Ser Asn Ser Ser Met Ser Asn 1735 1740 1745	5469		
70	AGC TAT TCC TAC CAT TCT GAT GAG GTA TAT AAT GAT TCA GGA TAT CTC Ser Tyr Ser Tyr His Ser Asp Glu Val Tyr Asn Asp Ser Gly Tyr Leu 1750 1755 1760	5517		
75	TCA AAA AAT AAA CTT GAT TCT GGT ATT GAG CCA GTA TTG AAG AAT GTT Ser Lys Asn Lys Leu Asp Ser Gly Ile Glu Pro Val Leu Lys Asn Val 1765 1770 1775	5565		

5	1780	GAA GAT CAA AAA AAC ACT AGT TTT TCC AAA GTA ATA TCC AAT GTA AAA	5613
		Glu Asp Gln Lys Asn Thr Ser Phe Ser Lys Val Ile Ser Asn Val Lys	
		1785 1790 1795	
10		GAT GCA AAT GCA TAC CCA CAA ACT GTA AAT GAA GAT ATT TGC GTT GAG	5661
		Asp Ala Asn Ala Tyr Pro Gln Thr Val Asn Glu Asp Ile Cys Val Glu	
		1800 1805 1810	
15		GAA CTT GTG ACT AGC TCT TCA CCC TGC AAA AAT AAA AAT GCA GCC ATT	5709
		Glu Leu Val Thr Ser Ser Ser Pro Cys Lys Asn Lys Asn Ala Ala Ile	
		1815 1820 1825	
20		AAA TTG TCC ATA TCT AAT AGT AAT AAT TTT GAG GTA GGG CCA CCT GCA	5757
		Lys Leu Ser Ile Ser Asn Ser Asn Asn Phe Glu Val Gly Pro Pro Ala	
		1830 1835 1840	
25		TTT AGG ATA GCC AGT GGT AAA ATC GTT TGT GTT TCA CAT GAA ACA ATT	5805
		Phe Arg Ile Ala Ser Gly Lys Ile Val Cys Val Ser His Glu Thr Ile	
		1845 1850 1855	
30		AAA AAA GTG AAA GAC ATA TTT ACA GAC AGT TTC AGT AAA GTA ATT AAG	5853
		Lys Lys Val Lys Asp Ile Phe Thr Asp Ser Phe Ser Lys Val Ile Lys	
		1860 1865 1870 1875	
35		GAA AAC AAC GAG AAT AAA TCA AAA ATT TGC CAA ACG AAA ATT ATG GCA	5901
		Glu Asn Asn Glu Asn Lys Ser Lys Ile Cys Gln Thr Lys Ile Met Ala	
		1880 1885 1890	
40		GGT TGT TAC GAG GCA TTG GAT GAT TCA GAG GAT ATT CTT CAT AAC TCT	5949
		Gly Cys Tyr Glu Ala Leu Asp Asp Ser Glu Asp Ile Leu His Asn Ser	
		1895 1900 1905	
45		CTA GAT AAT GAT GAA TGT AGC ACG CAT TCA CAT AAG GTT TTT GCT GAC	5997
		Leu Asp Asn Asp Glu Cys Ser Thr His Ser His Lys Val Phe Ala Asp	
		1910 1915 1920	
50		ATT CAG AGT GAA GAA ATT TTA CAA CAT AAC CAA AAT ATG TCT GGA TTG	6045
		Ile Gln Ser Glu Glu Ile Leu Gln His Asn Gln Asn Met Ser Gly Leu	
		1925 1930 1935	
55		GAG AAA GTT TCT AAA ATA TCA CCT TGT GAT GTT AGT TTG GAA ACT TCA	6093
		Glu Lys Val Ser Lys Ile Ser Pro Cys Asp Val Ser Leu Glu Thr Ser	
		1940 1945 1950 1955	
60		GAT ATA TGT AAA TGT AGT ATA GGG AAG CTT CAT AAG TCA GTC TCA TCT	6141
		Asp Ile Cys Lys Cys Ser Ile Gly Lys Leu His Lys Ser Val Ser Ser	
		1960 1965 1970	
65		GCA AAT ACT TGT GGG ATT TTT AGC ACA GCA AGT GGA AAA TCT GTC CAG	6189
		Ala Asn Thr Cys Gly Ile Phe Ser Thr Ala Ser Gly Lys Ser Val Gln	
		1975 1980 1985	
70		GTA TCA GAT GCT TCA TTA CAA AAC GCA AGA CAA GTG TTT TCT GAA ATA	6237
		Val Ser Asp Ala Ser Leu Gln Asn Ala Arg Gln Val Phe Ser Glu Ile	
		1990 1995 2000	
75		GAA GAT AGT ACC AAG CAA GTC TTT TCC AAA GTA TTG TTT AAA AGT AAC	6285
		Glu Asp Ser Thr Lys Gln Val Phe Ser Lys Val Leu Phe Lys Ser Asn	
		2005 2010 2015	

	GAA CAT TCA GAC CAG CTC ACA AGA GAA GAA AAT ACT GCT ATA CGT ACT Glu His Ser Asp Gln Leu Thr Arg Glu Glu Asn Thr Ala Ile Arg Thr 2020 2025 2030 2035	6333
5	CCA GAA CAT TTA ATA TCC CAA AAA GGC TTT TCA TAT AAT GTG GTA AAT Pro Glu His Leu Ile Ser Gln Lys Gly Phe Ser Tyr Asn Val Val Asn 2040 2045 2050	6381
10	TCA TCT GCT TTC TCT GGA TTT AGT ACA GCA AGT GGA AAG CAA GTT TCC Ser Ser Ala Phe Ser Gly Phe Ser Thr Ala Ser Gly Lys Gln Val Ser 2055 2060 2065	6429
15	ATT TTA GAA AGT TCC TTA CAC AAA GTT AAG GGA GTG TTA GAG GAA TTT Ile Leu Glu Ser Ser Leu His Lys Val Lys Gly Val Leu Glu Glu Phe 2070 2075 2080	6477
20	GAT TTA ATC AGA ACT GAG CAT AGT CTT CAC TAT TCA CCT ACG TCT AGA Asp Leu Ile Arg Thr Glu His Ser Leu His Tyr Ser Pro Thr Ser Arg 2085 2090 2095	6525
25	CAA AAT GTA TCA AAA ATA CTT CCT CGT GTT GAT AAG AGA AAC CCA GAG Gln Asn Val Ser Lys Ile Leu Pro Arg Val Asp Lys Arg Asn Pro Glu 2100 2105 2110 2115	6573
	CAC TGT GTA AAC TCA GAA ATG GAA AAA ACC TGC AGT AAA GAA TTT AAA His Cys Val Asn Ser Glu Met Glu Lys Thr Cys Ser Lys Glu Phe Lys 2120 2125 2130	6621
30	TTA TCA AAT AAC TTA AAT GTT GAA GGT GGT TCT TCA GAA AAT AAT CAC Leu Ser Asn Asn Leu Asn Val Glu Gly Gly Ser Ser Glu Asn Asn His 2135 2140 2145	6669
35	TCT ATT AAA GTT TCT CCA TAT CTC TCT CAA TTT CAA CAA GAC AAA CAA Ser Ile Lys Val Ser Pro Tyr Leu Ser Gln Phe Gln Gln Asp Lys Gln 2150 2155 2160	6717
40	CAG TTG GTA TTA GGA ACC AAA GTC TCA CTT GTT GAG AAC ATT CAT GTT Gln Leu Val Leu Gly Thr Lys Val Ser Leu Val Glu Asn Ile His Val 2165 2170 2175	6765
45	TTG GGA AAA GAA CAG GCT TCA CCT AAA AAC GTA AAA ATG GAA ATT GGT Leu Gly Lys Glu Gln Ala Ser Pro Lys Asn Val Lys Met Glu Ile Gly 2180 2185 2190 2195	6813
	AAA ACT GAA ACT TTT TCT GAT GTT CCT GTG AAA ACA AAT ATA GAA GTT Lys Thr Glu Thr Phe Ser Asp Val Pro Val Lys Thr Asn Ile Glu Val 2200 2205 2210	6861
50	TGT TCT ACT TAC TCC AAA GAT TCA GAA AAC TAC TTT GAA ACA GAA GCA Cys Ser Thr Tyr Ser Lys Asp Ser Glu Asn Tyr Phe Glu Thr Glu Ala 2215 2220 2225	6909
55	GTA GAA ATT GCT AAA GCT TTT ATG GAA GAT GAT GAA CTG ACA GAT TCT Val Glu Ile Ala Lys Ala Phe Met Glu Asp Asp Glu Leu Thr Asp Ser 2230 2235 2240	6957
60	AAA CTG CCA AGT CAT GCC ACA CAT TCT CTT TTT ACA TGT CCC GAA AAT Lys Leu Pro Ser His Ala Thr His Ser Leu Phe Thr Cys Pro Glu Asn 2245 2250 2255	7005
	GAG GAA ATG GTT TTG TCA AAT TCA AGA ATT GGA AAA AGA AGA GGA GAG	7053



	Glu Glu Met Val Leu Ser Asn Ser Arg Ile Gly Lys Arg Arg Gly Glu	
	2260 2265 2270 2275	
5	CCC CTT ATC TTA GTG GGA GAA CCC TCA ATC AAA AGA AAC TTA TTA AAT Pro Leu Ile Leu Val Gly Glu Pro Ser Ile Lys Arg Asn Leu Leu Asn	7101
	2280 2285 2290	
10	GAA TTT GAC AGG ATA ATA GAA AAT CAA GAA AAA TCC TTA AAG GCT TCA Glu Phe Asp Arg Ile Ile Glu Asn Gln Glu Lys Ser Leu Lys Ala Ser	7149
	2295 2300 2305	
15	AAA AGC ACT CCA GAT GGC ACA ATA AAA GAT CGA AGA TTG TTT ATG CAT Lys Ser Thr Pro Asp Gly Thr Ile Lys Asp Arg Arg Leu Phe Met His	7197
	2310 2315 2320	
20	CAT GTT TCT TTA GAG CCG ATT ACC TGT GTA CCC TTT CGC ACA ACT AAG His Val Ser Leu Glu Pro Ile Thr Cys Val Pro Phe Arg Thr Thr Lys	7245
	2325 2330 2335	
25	GAA CGT CAA GAG ATA CAG AAT CCA AAT TTT ACC GCA CCT GGT CAA GAA Glu Arg Gln Glu Ile Gln Asn Pro Asn Phe Thr Ala Pro Gly Gln Glu	7293
	2340 2345 2350 2355	
30	TTT CTG TCT AAA TCT CAT TTG TAT GAA CAT CTG ACT TTG GAA AAA TCT Phe Leu Ser Lys Ser His Leu Tyr Glu His Leu Thr Leu Glu Lys Ser	7341
	2360 2365 2370	
35	TCA AGC AAT TTA GCA GTT TCA GGA CAT CCA TTT TAT CAA GTT TCT GCT Ser Ser Asn Leu Ala Val Ser Gly His Pro Phe Tyr Gln Val Ser Ala	7389
	2375 2380 2385	
40	ACA AGA AAT GAA AAA ATG AGA CAC TTG ATT ACT ACA GGC AGA CCA ACC Thr Arg Asn Glu Lys Met Arg His Leu Ile Thr Thr Gly Arg Pro Thr	7437
	2390 2395 2400	
45	AAA GTC TTT GTT CCA CCT TTT AAA ACT AAA TCG CAT TTT CAC AGA GTT Lys Val Phe Val Pro Pro Phe Lys Thr Lys Ser His Phe His Arg Val	7485
	2405 2410 2415	
50	GAA CAG TGT GTT AGG AAT ATT AAC TTG GAG GAA AAC AGA CAA AAG CAA Glu Gln Cys Val Arg Asn Ile Asn Leu Glu Glu Asn Arg Gln Lys Gln	7533
	2420 2425 2430 2435	
55	AAC ATT GAT GGA CAT GGC TCT GAT GAT AGT AAA AAT AAG ATT AAT GAC Asn Ile Asp Gly His Gly Ser Asp Asp Ser Lys Asn Lys Ile Asn Asp	7581
	2440 2445 2450	
60	AAT GAG ATT CAT CAG TTT AAC AAA AAC AAC TCC AAT CAA GCA GCA GCT Asn Glu Ile His Gln Phe Asn Lys Asn Asn Ser Asn Gln Ala Ala Ala	7629
	2455 2460 2465	
65	GTA ACT TTC ACA AAG TGT GAA GAA GAA CCT TTA GAT TTA ATT ACA AGT Val Thr Phe Thr Lys Cys Glu Glu Glu Pro Leu Asp Leu Ile Thr Ser	7677
	2470 2475 2480	
70	CTT CAG AAT GCC AGA GAT ATA CAG GAT ATG CGA ATT AAG AAG AAA CAA Leu Gln Asn Ala Arg Asp Ile Gln Asp Met Arg Ile Lys Lys Lys Gln	7725
	2485 2490 2495	
75	AGG CAA CGC GTC TTT CCA CAG CCA GGC AGT CTG TAT CTT GCA AAA ACA Arg Gln Arg Val Phe Pro Gln Pro Gly Ser Leu Tyr Leu Ala Lys Thr	7773

	2500	2505	2510	2515	
5	TCC ACT CTG CCT CGA ATC TCT CTG AAA GCA GCA GTA GGA GGC CAA GTT Ser Thr Leu Pro Arg Ile Ser Leu Lys Ala Ala Val Gly Gly Gln Val	2520	2525	2530	7821
10	CCC TCT GCG TGT TCT CAT AAA CAG CTG TAT ACG TAT GGC GTT TCT AAA Pro Ser Ala Cys Ser His Lys Gln Leu Tyr Thr Tyr Gly Val Ser Lys	2535	2540	2545	7869
15	CAT TGC ATA AAA ATT AAC AGC AAA AAT GCA GAG TCT TTT CAG TTT CAC His Cys Ile Lys Ile Asn Ser Lys Asn Ala Glu Ser Phe Gln Phe His	2550	2555	2560	7917
20	ACT GAA GAT TAT TTT GGT AAG GAA AGT TTA TGG ACT GGA AAA GGA ATA Thr Glu Asp Tyr Phe Gly Lys Glu Ser Leu Trp Thr Gly Lys Gly Ile	2565	2570	2575	7965
25	CAG TTG GCT GAT GGT GGA TGG CTC ATA CCC ACC AAT GAT GGA AAG GCT Gln Leu Ala Asp Gly Gly Trp Leu Ile Pro Ser Asn Asp Gly Lys Ala	2580	2585	2590	8013
30	GGA AAA GAA GAA TTT TAT AGG GCT CTG TGT GAC ACT CCA GGT GTG GAT Gly Lys Glu Glu Phe Tyr Arg Ala Leu Cys Asp Thr Pro Gly Val Asp	2600	2605	2610	8061
35	CCA AAG CTT ATT TCT AGA ATT TGG GTT TAT AAT CAC TAT AGA TGG ATC Pro Lys Leu Ile Ser Arg Ile Trp Val Tyr Asn His Tyr Arg Trp Ile	2615	2620	2625	8109
40	ATA TGG AAA CTG GCA GCT ATG GAA TGT GCC TTT CCT AAG GAA TTT GCT Ile Trp Lys Leu Ala Ala Met Glu Cys Ala Phe Pro Lys Glu Phe Ala	2630	2635	2640	8157
45	AAT AGA TGC CTA AGC CCA GAA AGG GTG CTT CTT CAA CTA AAA TAC AGA Asn Arg Cys Leu Ser Pro Glu Arg Val Leu Leu Gln Leu Lys Tyr Arg	2645	2650	2655	8205
50	TAT GAT ACG GAA ATT GAT AGA AGC AGA AGA TCG GCT ATA AAA AAG ATA Tyr Asp Thr Glu Ile Asp Arg Ser Arg Arg Ser Ala Ile Lys Lys Ile	2660	2665	2670	8253
55	ATG GAA AGG GAT GAC ACA GCT GCA AAA ACA CTT GTT CTC TGT GTT TCT Met Glu Arg Asp Asp Thr Ala Ala Lys Thr Leu Val Leu Cys Val Ser	2680	2685	2690	8301
60	GAC ATA ATT TCA TTG AGC GCA AAT ATA TCT GAA ACT TCT AGC AAT AAA Asp Ile Ile Ser Leu Ser Ala Asn Ile Ser Glu Thr Ser Ser Asn Lys	2695	2700	2705	8349
	ACT AGT AGT GCA GAT ACC CAA AAA GTG GCC ATT ATT GAA CTT ACA GAT Thr Ser Ser Ala Asp Thr Gln Lys Val Ala Ile Ile Glu Leu Thr Asp	2710	2715	2720	8397
	GGG TGG TAT GCT GTT AAG GCC CAG TTA GAT CCT CCC CTC TTA GCT GTC Gly Trp Tyr Ala Val Lys Ala Gln Leu Asp Pro Pro Leu Leu Ala Val	2725	2730	2735	8445
	TTA AAG AAT GGC AGA CTG ACA GTT GGT CAG AAG ATT ATT CTT CAT GGA Leu Lys Asn Gly Arg Leu Thr Val Gly Gln Lys Ile Ile Leu His Gly	2740	2745	2750	8493

5	GCA GAA CTG GTG GGC TCT CCT GAT GCC TGT ACA CCT CTT GAA GCC CCA Ala Glu Leu Val Gly Ser Pro Asp Ala Cys Thr Pro Leu Glu Ala Pro 2760 2765 2770	8541
10	GAA TCT CTT ATG TTA AAG ATT TCT GCT AAC AGT ACT CGG CCT GCT CGC Glu Ser Leu Met Leu Lys Ile Ser Ala Asn Ser Thr Arg Pro Ala Arg 2775 2780 2785	8589
15	TGG TAT ACC AAA CTT GGA TTC TTT CCT GAC CCT AGA CCT TTT CCT CTG Trp Tyr Thr Lys Leu Gly Phe Phe Pro Asp Pro Arg Pro Phe Pro Leu 2790 2795 2800	8637
20	CCC TTA TCA TCG CTT TTC AGT GAT GGA GGA AAT GTT GGT TGT GTT GAT Pro Leu Ser Ser Leu Phe Ser Asp Gly Gly Asn Val Gly Cys Val Asp 2805 2810 2815	8685
25	GTA ATT ATT CAA AGA GCA TAC CCT ATA CAG TGG ATG GAG AAG ACA TCA Val Ile Ile Gln Arg Ala Tyr Pro Ile Gln Trp Met Glu Lys Thr Ser 2820 2825 2830 2835	8733
30	TCT GGA TTA TAC ATA TTT CGC AAT GAA AGA GAG GAA GAA AAG GAA GCA Ser Gly Leu Tyr Ile Phe Arg Asn Glu Arg Glu Glu Glu Lys Glu Ala 2840 2845 2850	8781
35	GCA AAA TAT GTG GAG GCC CAA CAA AAG AGA CTA GAA GCC TTA TTC ACT Ala Lys Tyr Val Glu Ala Gln Gln Lys Arg Leu Glu Ala Leu Phe Thr 2855 2860 2865	8829
40	AAA ATT CAG GAG GAA TTT GAA GAA CAT GAA GAA AAC ACA ACA AAA CCA Lys Ile Gln Glu Glu Phe Glu Glu His Glu Glu Asn Thr Thr Lys Pro 2870 2875 2880	8877
45	TAT TTA CCA TCA CGT GCA CTA ACA AGA CAG CAA GTT CGT GCT TTG CAA Tyr Leu Pro Ser Arg Ala Leu Thr Arg Gln Gln Val Arg Ala Leu Gln 2885 2890 2895	8925
50	GAT GGT GCA GAG CTT TAT GAA GCA GTG AAG AAT GCA GCA GAC CCA GCT Asp Gly Ala Glu Leu Tyr Glu Ala Val Lys Asn Ala Ala Asp Pro Ala 2900 2905 2910 2915	8973
55	TAC CTT GAG GGT TAT TTC AGT GAA GAG CAG TTA AGA GCC TTG AAT AAT Tyr Leu Glu Gly Tyr Phe Ser Glu Glu Gln Leu Arg Ala Leu Asn Asn 2920 2925 2930	9021
60	CAC AGG CAA ATG TTG AAT GAT AAG AAA CAA GCT CAG ATC CAG TTG GAA His Arg Gln Met Leu Asn Asp Lys Lys Gln Ala Gln Ile Gln Leu Glu 2935 2940 2945	9069
65	ATT AGG AAG GCC ATG GAA TCT GCT GAA CAA AAG GAA CAA GGT TTA TCA Ile Arg Lys Ala Met Glu Ser Ala Glu Gln Lys Glu Gln Gly Leu Ser 2950 2955 2960	9117
70	AGG GAT GTC ACA ACC GTG TGG AAG TTG CGT ATT GTA AGC TAT TCA AAA Arg Asp Val Thr Thr Val Trp Lys Leu Arg Ile Val Ser Tyr Ser Lys 2965 2970 2975	9165
75	AAA GAA AAA GAT TCA GTT ATA CTG AGT ATT TGG CGT CCA TCA TCA GAT Lys Glu Lys Asp Ser Val Ile Leu Ser Ile Trp Arg Pro Ser Ser Asp 2980 2985 2990 2995	9213

	TTA TAT TCT CTG TTA ACA GAA GGA AAG AGA TAC AGA ATT TAT CAT CTT Leu Tyr Ser Leu Leu Thr Glu Gly Lys Arg Tyr Arg Ile Tyr His Leu 3000 3005 3010	9261
5	GCA ACT TCA AAA TCT AAA AGT AAA TCT GAA AGA GCT AAC ATA CAG TTA Ala Thr Ser Lys Ser Lys Ser Lys Ser Glu Arg Ala Asn Ile Gln Leu 3015 3020 3025	9309
10	GCA GCG ACA AAA AAA ACT CAG TAT CAA CAA CTA CCG GTT TCA GAT GAA Ala Ala Thr Lys Lys Thr Gln Tyr Gln Gln Leu Pro Val Ser Asp Glu 3030 3035 3040	9357
15	ATT TTA TTT CAG ATT TAC CAG CCA CGG GAG CCC CTT CAC TTC AGC AAA Ile Leu Phe Gln Ile Tyr Gln Pro Arg Glu Pro Leu His Phe Ser Lys 3045 3050 3055	9405
20	TTT TTA GAT CCA GAC TTT CAG CCA TCT TGT TCT GAG GTG GAC CTA ATA Phe Leu Asp Pro Asp Phe Gln Pro Ser Cys Ser Glu Val Asp Leu Ile 3060 3065 3070 3075	9453
25	GGA TTT GTC GTT TCT GTT GTG AAA AAA ACA GGA CTT GCC CCT TTC GTC Gly Phe Val Val Ser Val Val Lys Lys Thr Gly Leu Ala Pro Phe Val 3080 3085 3090	9501
30	TAT TTG TCA GAC GAA TGT TAC AAT TTA CTG GCA ATA AAG TTT TGG ATA Tyr Leu Ser Asp Glu Cys Tyr Asn Leu Leu Ala Ile Lys Phe Trp Ile 3095 3100 3105	9549
35	GAC CTT AAT GAG GAC ATT ATT AAG CCT CAT ATG TTA ATT GCT GCA AGC Asp Leu Asn Glu Asp Ile Ile Lys Pro His Met Leu Ile Ala Ala Ser 3110 3115 3120	9597
40	AAC CTC CAG TGG CGA CCA GAA TCC AAA TCA GGC CTT CTT ACT TTA TTT Asn Leu Gln Trp Arg Pro Glu Ser Lys Ser Gly Leu Leu Thr Leu Phe 3125 3130 3135	9645
45	GCT GGA GAT TTT TCT GTG TTT TCT GCT AGT CCA AAA GAG GGC CAC TTT Ala Gly Asp Phe Ser Val Phe Ser Ala Ser Pro Lys Glu Gly His Phe 3140 3145 3150 3155	9693
50	CAA GAG ACA TTC AAC AAA ATG AAA AAT ACT GTT GAG AAT ATT GAC ATA Gln Glu Thr Phe Asn Lys Met Lys Asn Thr Val Glu Asn Ile Asp Ile 3160 3165 3170	9741
55	CTT TGC AAT GAA GCA GAA AAC AAG CTT ATG CAT ATA CTG CAT GCA AAT Leu Cys Asn Glu Ala Glu Asn Lys Leu Met His Ile Leu His Ala Asn 3175 3180 3185	9789
60	GAT CCC AAG TGG TCC ACC CCA ACT AAA GAC TGT ACT TCA GGG CCG TAC Asp Pro Lys Trp Ser Thr Pro Thr Lys Asp Cys Thr Ser Gly Pro Tyr 3190 3195 3200	9837
	ACT GCT CAA ATC ATT CCT GGT ACA GGA AAC AAG CTT CTG ATG TCT TCT Thr Ala Gln Ile Ile Pro Gly Thr Gly Asn Lys Leu Leu Met Ser Ser 3205 3210 3215	9885
	CCT AAT TGT GAG ATA TAT TAT CAA AGT CCT TTA TCA CTT TGT ATG GCC Pro Asn Cys Glu Ile Tyr Tyr Gln Ser Pro Leu Ser Leu Cys Met Ala 3220 3225 3230 3235	9933
	AAA AGG AAG TCT GTT TCC ACA CCT GTC TCA GCC CAG ATG ACT TCA AAG	9981

	Lys Arg Lys Ser Val Ser Thr Pro Val Ser Ala Gln Met Thr Ser Lys	
	3240 3245 3250	
5	TCT TGT AAA GGG GAG AAA GAG ATT GAT GAC CAA AAG AAC TGC AAA AAG Ser Cys Lys Gly Glu Lys Glu Ile Asp Asp Gln Lys Asn Cys Lys Lys	10029
	3255 3260 3265	
10	AGA AGA GCC TTG GAT TTC TTG AGT AGA CTG CCT TTA CCT CCA CCT GTT Arg Arg Ala Leu Asp Phe Leu Ser Arg Leu Pro Leu Pro Pro Pro Val	10077
	3270 3275 3280	
15	AGT CCC ATT TGT ACA TTT GTT TCT CCG GCT GCA CAG AAG GCA TTT CAG Ser Pro Ile Cys Thr Phe Val Ser Pro Ala Ala Gln Lys Ala Phe Gln	10125
	3285 3290 3295	
20	CCA CCA AGG AGT TCT GGC ACC AAA TAC GAA ACA CCC ATA AAG AAA AAA Pro Pro Arg Ser Cys Gly Thr Lys Tyr Glu Thr Pro Ile Lys Lys Lys	10173
	3300 3305 3310 3315	
25	GAA CTG AAT TCT CCT CAG ATG ACT CCA TTT AAA AAA TTC AAT GAA ATT Glu Leu Asn Ser Pro Gln Met Thr Pro Phe Lys Lys Phe Asn Glu Ile	10221
	3320 3325 3330	
30	TCT CTT TTG GAA AGT AAT TCA ATA GCA GAC GAA GAA CTT GCA TTG ATA Ser Leu Leu Glu Ser Asn Ser Ile Ala Asp Glu Glu Leu Ala Leu Ile	10269
	3335 3340 3345	
35	AAT ACC CAA GCT CTT TTG TCT GGT TCA ACA GGA GAA AAA CAA TTT ATA Asn Thr Gln Ala Leu Leu Ser Gly Ser Thr Gly Glu Lys Gln Phe Ile	10317
	3350 3355 3360	
40	TCT GTC AGT GAA TCC ACT AGG ACT GCT CCC ACC AGT TCA GAA GAT TAT Ser Val Ser Glu Ser Thr Arg Thr Ala Pro Thr Ser Ser Glu Asp Tyr	10365
	3365 3370 3375	
45	CTC AGA CTG AAA CGA CGT TGT ACT ACA TCT CTG ATC AAA GAA CAG GAG Leu Arg Leu Lys Arg Arg Cys Thr Thr Ser Leu Ile Lys Glu Gln Glu	10413
	3380 3385 3390 3395	
50	AGT TCC CAG GCC AGT ACG GAA GAA TGT GAG AAA AAT AAG CAG GAC ACA Ser Ser Gln Ala Ser Thr Glu Glu Cys Glu Lys Asn Lys Gln Asp Thr	10461
	3400 3405 3410	
55	ATT ACA ACT AAA AAA TAT ATC TAA Ile Thr Thr Lys Lys Tyr Ile	10485
	3415	

50 (2) INFORMATION FOR SEQ ID NO:9:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 3418 amino acids  
 (B) TYPE: amino acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

55 (ii) MOLECULE TYPE: protein  
 (v) FRAGMENT TYPE: internal

60 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

Met Pro Ile Gly Ser Lys Glu Arg Pro Thr Phe Phe Glu Ile Phe Lys  
 1 5 10 15  
 5 Thr Arg Cys Asn Lys Ala Asp Leu Gly Pro Ile Ser Leu Asn Trp Phe  
 20 25 30  
 Glu Glu Leu Ser Ser Glu Ala Pro Pro Tyr Asn Ser Glu Pro Ala Glu  
 35 40 45  
 Glu Ser Glu His Lys Asn Asn Asn Tyr Glu Pro Asn Leu Phe Lys Thr  
 50 55 60  
 10 Pro Gln Arg Lys Pro Ser Tyr Asn Gln Leu Ala Ser Thr Pro Ile Ile  
 65 70 75 80  
 Phe Lys Glu Gln Gly Leu Thr Leu Pro Leu Tyr Gln Ser Pro Val Lys  
 85 90 95  
 Glu Leu Asp Lys Phe Lys Leu Asp Leu Gly Arg Asn Val Pro Asn Ser  
 100 105 110  
 15 Arg His Lys Ser Leu Arg Thr Val Lys Thr Lys Met Asp Gln Ala Asp  
 115 120 125  
 Asp Val Ser Cys Pro Leu Leu Asn Ser Cys Leu Ser Glu Ser Pro Val  
 130 135 140  
 20 Val Leu Gln Cys Thr His Val Thr Pro Gln Arg Asp Lys Ser Val Val  
 145 150 155 160  
 Cys Gly Ser Leu Phe His Thr Pro Lys Phe Val Lys Gly Arg Gln Thr  
 165 170 175  
 Pro Lys His Ile Ser Glu Ser Leu Gly Ala Glu Val Asp Pro Asp Met  
 180 185 190  
 25 Ser Trp Ser Ser Ser Leu Ala Thr Pro Pro Thr Leu Ser Ser Thr Val  
 195 200 205  
 Leu Ile Val Arg Asn Glu Glu Ala Ser Glu Thr Val Phe Pro His Asp  
 210 215 220  
 30 Thr Thr Ala Asn Val Lys Ser Tyr Phe Ser Asn His Asp Glu Ser Leu  
 225 230 235 240  
 Lys Lys Asn Asp Arg Phe Ile Ala Ser Val Thr Asp Ser Glu Asn Thr  
 245 250 255  
 Asn Gln Arg Glu Ala Ala Ser His Gly Phe Gly Lys Thr Ser Gly Asn  
 260 265 270  
 35 Ser Phe Lys Val Asn Ser Cys Lys Asp His Ile Gly Lys Ser Met Pro  
 275 280 285  
 His Val Leu Glu Asp Glu Val Tyr Glu Thr Val Val Asp Thr Ser Glu  
 290 295 300  
 40 Glu Asp Ser Phe Ser Leu Cys Phe Ser Lys Cys Arg Thr Lys Asn Leu  
 305 310 315 320  
 Gln Lys Val Arg Thr Ser Lys Thr Arg Lys Lys Ile Phe His Glu Ala  
 325 330 335  
 Asn Ala Asp Glu Cys Glu Lys Ser Lys Asn Gln Val Lys Glu Lys Tyr  
 340 345 350  
 45 Ser Phe Val Ser Glu Val Glu Pro Asn Asp Thr Asp Pro Leu Asp Ser  
 355 360 365  
 Asn Val Ala Asn Gln Lys Pro Phe Glu Ser Gly Ser Asp Lys Ile Ser  
 370 375 380  
 50 Lys Glu Val Val Pro Ser Leu Ala Cys Glu Trp Ser Gln Leu Thr Leu  
 385 390 395 400  
 Ser Gly Leu Asn Gly Ala Gln Met Glu Lys Ile Pro Leu Leu His Ile  
 405 410 415  
 Ser Ser Cys Asp Gln Asn Ile Ser Glu Lys Asp Leu Leu Asp Thr Glu  
 420 425 430  
 55 Asn Lys Arg Lys Lys Asp Phe Leu Thr Ser Glu Asn Ser Leu Pro Arg  
 435 440 445  
 Ile Ser Ser Leu Pro Lys Ser Glu Lys Pro Leu Asn Glu Glu Thr Val  
 450 455 460  
 60 Val Asn Lys Arg Asp Glu Glu Gln His Leu Glu Ser His Thr Asp Cys  
 465 470 475 480  
 Ile Leu Ala Val Lys Gln Ala Ile Ser Gly Thr Ser Pro Val Ala Ser

				485				490					495				
	Ser	Phe	Gln	Gly	Ile	Lys	Lys	Ser	Ile	Phe	Arg	Ile	Arg	Glu	Ser	Pro	
				500					505					510			
5	Lys	Glu	Thr	Phe	Asn	Ala	Ser	Phe	Ser	Gly	His	Met	Thr	Asp	Pro	Asn	
			515						520				525				
	Phe	Lys	Lys	Glu	Thr	Glu	Ala	Ser	Glu	Ser	Gly	Leu	Glu	Ile	His	Thr	
		530					535					540					
10	Val	Cys	Ser	Gln	Lys	Glu	Asp	Ser	Leu	Cys	Pro	Asn	Leu	Ile	Asp	Asn	
	545					550					555				560		
	Gly	Ser	Trp	Pro	Ala	Thr	Thr	Thr	Gln	Asn	Ser	Val	Ala	Leu	Lys	Asn	
				565						570					575		
	Ala	Gly	Leu	Ile	Ser	Thr	Leu	Lys	Lys	Lys	Thr	Asn	Lys	Phe	Ile	Tyr	
			580						585					590			
15	Ala	Ile	His	Asp	Glu	Thr	Ser	Tyr	Lys	Gly	Lys	Lys	Ile	Pro	Lys	Asp	
			595					600					605				
	Gln	Lys	Ser	Glu	Leu	Ile	Asn	Cys	Ser	Ala	Gln	Phe	Glu	Ala	Asn	Ala	
		610					615						620				
20	Phe	Glu	Ala	Pro	Leu	Thr	Phe	Ala	Asn	Ala	Asp	Ser	Gly	Leu	Leu	His	
	625					630					635					640	
	Ser	Ser	Val	Lys	Arg	Ser	Cys	Ser	Gln	Asn	Asp	Ser	Glu	Glu	Pro	Thr	
				645						650					655		
	Leu	Ser	Leu	Thr	Ser	Ser	Phe	Gly	Thr	Ile	Leu	Arg	Lys	Cys	Ser	Arg	
				660					665					670			
25	Asn	Glu	Thr	Cys	Ser	Asn	Asn	Thr	Val	Ile	Ser	Gln	Asp	Leu	Asp	Tyr	
			675					680					685				
	Lys	Glu	Ala	Lys	Cys	Asn	Lys	Glu	Lys	Leu	Gln	Leu	Phe	Ile	Thr	Pro	
		690					695					700					
30	Glu	Ala	Asp	Ser	Leu	Ser	Cys	Leu	Gln	Glu	Gly	Gln	Cys	Glu	Asn	Asp	
	705					710					715				720		
	Pro	Lys	Ser	Lys	Lys	Val	Ser	Asp	Ile	Lys	Glu	Glu	Val	Leu	Ala	Ala	
				725						730					735		
	Ala	Cys	His	Pro	Val	Gln	His	Ser	Lys	Val	Glu	Tyr	Ser	Asp	Thr	Asp	
			740						745					750			
35	Phe	Gln	Ser	Gln	Lys	Ser	Leu	Leu	Tyr	Asp	His	Glu	Asn	Ala	Ser	Thr	
			755					760					765				
	Leu	Ile	Leu	Thr	Pro	Thr	Ser	Lys	Asp	Val	Leu	Ser	Asn	Leu	Val	Met	
			770				775					780					
40	Ile	Ser	Arg	Gly	Lys	Glu	Ser	Tyr	Lys	Met	Ser	Asp	Lys	Leu	Lys	Gly	
	785					790					795					800	
	Asn	Asn	Tyr	Glu	Ser	Asp	Val	Glu	Leu	Thr	Lys	Asn	Ile	Pro	Met	Glu	
				805						810					815		
	Lys	Asn	Gln	Asp	Val	Cys	Ala	Leu	Asn	Glu	Asn	Tyr	Lys	Asn	Val	Glu	
			820						825					830			
45	Leu	Leu	Pro	Pro	Glu	Lys	Tyr	Met	Arg	Val	Ala	Ser	Pro	Ser	Arg	Lys	
			835					840					845				
	Val	Gln	Phe	Asn	Gln	Asn	Thr	Asn	Leu	Arg	Val	Ile	Gln	Lys	Asn	Gln	
		850				855						860					
50	Glu	Glu	Thr	Thr	Ser	Ile	Ser	Lys	Ile	Thr	Val	Asn	Pro	Asp	Ser	Glu	
	865					870					875					880	
	Glu	Leu	Phe	Ser	Asp	Asn	Glu	Asn	Asn	Phe	Val	Phe	Gln	Val	Ala	Asn	
				885						890					895		
	Glu	Arg	Asn	Asn	Leu	Ala	Leu	Gly	Asn	Thr	Lys	Glu	Leu	His	Glu	Thr	
				900					905					910			
55	Asp	Leu	Thr	Cys	Val	Asn	Glu	Pro	Ile	Phe	Lys	Asn	Ser	Thr	Met	Val	
			915					920					925				
	Leu	Tyr	Gly	Asp	Thr	Gly	Asp	Lys	Gln	Ala	Thr	Gln	Val	Ser	Ile	Lys	
		930					935					940					
60	Lys	Asp	Leu	Val	Tyr	Val	Leu	Ala	Glu	Glu	Asn	Lys	Asn	Ser	Val	Lys	
	945					950					955					960	
	Gln	His	Ile	Lys	Met	Thr	Leu	Gly	Gln	Asp	Leu	Lys	Ser	Asp	Ile	Ser	
				965					970						975		

Leu Asn Ile Asp Lys Ile Pro Glu Lys Asn Asn Asp Tyr Met Asp Lys  
 980 985 990  
 5 Trp Ala Gly Leu Leu Gly Pro Ile Ser Asn His Ser Phe Gly Gly Ser  
 995 1000 1005  
 Phe Arg Thr Ala Ser Asn Lys Glu Ile Lys Leu Ser Glu His Asn Ile  
 1010 1015 1020  
 Lys Lys Ser Lys Met Phe Phe Lys Asp Ile Glu Glu Gln Tyr Pro Thr  
 1025 1030 1035 104  
 10 Ser Leu Ala Cys Val Glu Ile Val Asn Thr Leu Ala Leu Asp Asn Gln  
 1045 1050 1055  
 Lys Lys Leu Ser Lys Pro Gln Ser Ile Asn Thr Val Ser Ala His Leu  
 1060 1065 1070  
 15 Gln Ser Ser Val Val Val Ser Asp Cys Lys Asn Ser His Ile Thr Pro  
 1075 1080 1085  
 Gln Met Leu Phe Ser Lys Gln Asp Phe Asn Ser Asn His Asn Leu Thr  
 1090 1095 1100  
 Pro Ser Gln Lys Ala Glu Ile Thr Glu Leu Ser Thr Ile Leu Glu Glu  
 1105 1110 1115 112  
 20 Ser Gly Ser Gln Phe Glu Phe Thr Gln Phe Arg Lys Pro Ser Tyr Ile  
 1125 1130 1135  
 Leu Gln Lys Ser Thr Phe Glu Val Pro Glu Asn Gln Met Thr Ile Leu  
 1140 1145 1150  
 25 Lys Thr Thr Ser Glu Glu Cys Arg Asp Ala Asp Leu His Val Ile Met  
 1155 1160 1165  
 Asn Ala Pro Ser Ile Gly Gln Val Asp Ser Ser Lys Gln Phe Glu Gly  
 1170 1175 1180  
 Thr Val Glu Ile Lys Arg Lys Phe Ala Gly Leu Leu Lys Asn Asp Cys  
 1185 1190 1195 120  
 30 Asn Lys Ser Ala Ser Gly Tyr Leu Thr Asp Glu Asn Glu Val Gly Phe  
 1205 1210 1215  
 Arg Gly Phe Tyr Ser Ala His Gly Thr Lys Leu Asn Val Ser Thr Glu  
 1220 1225 1230  
 35 Ala Leu Gln Lys Ala Val Lys Leu Phe Ser Asp Ile Glu Asn Ile Ser  
 1235 1240 1245  
 Glu Glu Thr Ser Ala Glu Val His Pro Ile Ser Leu Ser Ser Ser Lys  
 1250 1255 1260  
 Cys His Asp Ser Val Val Ser Met Phe Lys Ile Glu Asn His Asn Asp  
 1265 1270 1275 128  
 40 Lys Thr Val Ser Glu Lys Asn Asn Lys Cys Gln Leu Ile Leu Gln Asn  
 1285 1290 1295  
 Asn Ile Glu Met Thr Thr Gly Thr Phe Val Glu Glu Ile Thr Glu Asn  
 1300 1305 1310  
 45 Tyr Lys Arg Asn Thr Glu Asn Glu Asp Asn Lys Tyr Thr Ala Ala Ser  
 1315 1320 1325  
 Arg Asn Ser His Asn Leu Glu Phe Asp Gly Ser Asp Ser Ser Lys Asn  
 1330 1335 1340  
 Asp Thr Val Cys Ile His Lys Asp Glu Thr Asp Leu Leu Phe Thr Asp  
 1345 1350 1355 136  
 50 Gln His Asn Ile Cys Leu Lys Leu Ser Gly Gln Phe Met Lys Glu Gly  
 1365 1370 1375  
 Asn Thr Gln Ile Lys Glu Asp Leu Ser Asp Leu Thr Phe Leu Glu Val  
 1380 1385 1390  
 55 Ala Lys Ala Gln Glu Ala Cys His Gly Asn Thr Ser Asn Lys Glu Gln  
 1395 1400 1405  
 Leu Thr Ala Thr Lys Thr Glu Gln Asn Ile Lys Asp Phe Glu Thr Ser  
 1410 1415 1420  
 Asp Thr Phe Phe Gln Thr Ala Ser Gly Lys Asn Ile Ser Val Ala Lys  
 1425 1430 1435 144  
 60 Glu Ser Phe Asn Lys Ile Val Asn Phe Phe Asp Gln Lys Pro Glu Glu  
 1445 1450 1455  
 Leu His Asn Phe Ser Leu Asn Ser Glu Leu His Ser Asp Ile Arg Lys



		1460		1465		1470	
		Asn Lys Met Asp Ile Leu Ser Tyr Glu Glu Thr Asp Ile Val Lys His					
		1475		1480		1485	
5		Lys Ile Leu Lys Glu Ser Val Pro Val Gly Thr Gly Asn Gln Leu Val					
		1490		1495		1500	
		Thr Phe Gln Gly Gln Pro Glu Arg Asp Glu Lys Ile Lys Glu Pro Thr					
		1505		1510		1515	152
		Leu Leu Gly Phe His Thr Ala Ser Gly Lys Lys Val Lys Ile Ala Lys					
10		1525		1530		1535	
		Glu Ser Leu Asp Lys Val Lys Asn Leu Phe Asp Glu Lys Glu Gln Gly					
		1540		1545		1550	
		Thr Ser Glu Ile Thr Ser Phe Ser His Gln Trp Ala Lys Thr Leu Lys					
		1555		1560		1565	
15		Tyr Arg Glu Ala Cys Lys Asp Leu Glu Leu Ala Cys Glu Thr Ile Glu					
		1570		1575		1580	
		Ile Thr Ala Ala Pro Lys Cys Lys Glu Met Gln Asn Ser Leu Asn Asn					
		1585		1590		1595	160
		Asp Lys Asn Leu Val Ser Ile Glu Thr Val Val Pro Pro Lys Leu Leu					
20		1605		1610		1615	
		Ser Asp Asn Leu Cys Arg Gln Thr Glu Asn Leu Lys Thr Ser Lys Ser					
		1620		1625		1630	
		Ile Phe Leu Lys Val Lys Val His Glu Asn Val Glu Lys Glu Thr Ala					
		1635		1640		1645	
25		Lys Ser Pro Ala Thr Cys Tyr Thr Asn Gln Ser Pro Tyr Ser Val Ile					
		1650		1655		1660	
		Glu Asn Ser Ala Leu Ala Phe Tyr Thr Ser Cys Ser Arg Lys Thr Ser					
		1665		1670		1675	168
		Val Ser Gln Thr Ser Leu Leu Glu Ala Lys Lys Trp Leu Arg Glu Gly					
30		1685		1690		1695	
		Ile Phe Asp Gly Gln Pro Glu Arg Ile Asn Thr Ala Asp Tyr Val Gly					
		1700		1705		1710	
		Asn Tyr Leu Tyr Glu Asn Asn Ser Asn Ser Thr Ile Ala Glu Asn Asp					
		1715		1720		1725	
35		Lys Asn His Leu Ser Glu Lys Gln Asp Thr Tyr Leu Ser Asn Ser Ser					
		1730		1735		1740	
		Met Ser Asn Ser Tyr Ser Tyr His Ser Asp Glu Val Tyr Asn Asp Ser					
		1745		1750		1755	176
		Gly Tyr Leu Ser Lys Asn Lys Leu Asp Ser Gly Ile Glu Pro Val Leu					
40		1765		1770		1775	
		Lys Asn Val Glu Asp Gln Lys Asn Thr Ser Phe Ser Lys Val Ile Ser					
		1780		1785		1790	
		Asn Val Lys Asp Ala Asn Ala Tyr Pro Gln Thr Val Asn Glu Asp Ile					
		1795		1800		1805	
45		Cys Val Glu Glu Leu Val Thr Ser Ser Ser Pro Cys Lys Asn Lys Asn					
		1810		1815		1820	
		Ala Ala Ile Lys Leu Ser Ile Ser Asn Ser Asn Asn Phe Glu Val Gly					
		1825		1830		1835	184
		Pro Pro Ala Phe Arg Ile Ala Ser Gly Lys Ile Val Cys Val Ser His					
50		1845		1850		1855	
		Glu Thr Ile Lys Lys Val Lys Asp Ile Phe Thr Asp Ser Phe Ser Lys					
		1860		1865		1870	
		Val Ile Lys Glu Asn Asn Glu Asn Lys Ser Lys Ile Cys Gln Thr Lys					
		1875		1880		1885	
55		Ile Met Ala Gly Cys Tyr Glu Ala Leu Asp Asp Ser Glu Asp Ile Leu					
		1890		1895		1900	
		His Asn Ser Leu Asp Asn Asp Glu Cys Ser Thr His Ser His Lys Val					
		1905		1910		1915	192
		Phe Ala Asp Ile Gln Ser Glu Glu Ile Leu Gln His Asn Gln Asn Met					
60		1925		1930		1935	
		Ser Gly Leu Glu Lys Val Ser Lys Ile Ser Pro Cys Asp Val Ser Leu					
		1940		1945		1950	

Glu Thr Ser Asp Ile Cys Lys Cys Ser Ile Gly Lys Leu His Lys Ser  
 1955 1960 1965  
 5 Val Ser Ser Ala Asn Thr Cys Gly Ile Phe Ser Thr Ala Ser Gly Lys  
 1970 1975 1980  
 Ser Val Gln Val Ser Asp Ala Ser Leu Gln Asn Ala Arg Gln Val Phe  
 1985 1990 1995 200  
 Ser Glu Ile Glu Asp Ser Thr Lys Gln Val Phe Ser Lys Val Leu Phe  
 2005 2010 2015  
 10 Lys Ser Asn Glu His Ser Asp Gln Leu Thr Arg Glu Glu Asn Thr Ala  
 2020 2025 2030  
 Ile Arg Thr Pro Glu His Leu Ile Ser Gln Lys Gly Phe Ser Tyr Asn  
 2035 2040 2045  
 Val Val Asn Ser Ser Ala Phe Ser Gly Phe Ser Thr Ala Ser Gly Lys  
 15 2050 2055 2060  
 Gln Val Ser Ile Leu Glu Ser Ser Leu His Lys Val Lys Gly Val Leu  
 2065 2070 2075 208  
 Glu Glu Phe Asp Leu Ile Arg Thr Glu His Ser Leu His Tyr Ser Pro  
 2085 2090 2095  
 20 Thr Ser Arg Gln Asn Val Ser Lys Ile Leu Pro Arg Val Asp Lys Arg  
 2100 2105 2110  
 Asn Pro Glu His Cys Val Asn Ser Glu Met Glu Lys Thr Cys Ser Lys  
 2115 2120 2125  
 25 Glu Phe Lys Leu Ser Asn Asn Leu Asn Val Glu Gly Gly Ser Ser Glu  
 2130 2135 2140  
 Asn Asn His Ser Ile Lys Val Ser Pro Tyr Leu Ser Gln Phe Gln Gln  
 2145 2150 2155 216  
 Asp Lys Gln Gln Leu Val Leu Gly Thr Lys Val Ser Leu Val Glu Asn  
 2165 2170 2175  
 30 Ile His Val Leu Gly Lys Glu Gln Ala Ser Pro Lys Asn Val Lys Met  
 2180 2185 2190  
 Glu Ile Gly Lys Thr Glu Thr Phe Ser Asp Val Pro Val Lys Thr Asn  
 2195 2200 2205  
 35 Ile Glu Val Cys Ser Thr Tyr Ser Lys Asp Ser Glu Asn Tyr Phe Glu  
 2210 2215 2220  
 Thr Glu Ala Val Glu Ile Ala Lys Ala Phe Met Glu Asp Asp Glu Leu  
 2225 2230 2235 224  
 Thr Asp Ser Lys Leu Pro Ser His Ala Thr His Ser Leu Phe Thr Cys  
 2245 2250 2255  
 40 Pro Glu Asn Glu Glu Met Val Leu Ser Asn Ser Arg Ile Gly Lys Arg  
 2260 2265 2270  
 Arg Gly Glu Pro Leu Ile Leu Val Gly Glu Pro Ser Ile Lys Arg Asn  
 2275 2280 2285  
 45 Leu Leu Asn Glu Phe Asp Arg Ile Ile Glu Asn Gln Glu Lys Ser Leu  
 2290 2295 2300  
 Lys Ala Ser Lys Ser Thr Pro Asp Gly Thr Ile Lys Asp Arg Arg Leu  
 2305 2310 2315 232  
 Phe Met His His Val Ser Leu Glu Pro Ile Thr Cys Val Pro Phe Arg  
 2325 2330 2335  
 50 Thr Thr Lys Glu Arg Gln Glu Ile Gln Asn Pro Asn Phe Thr Ala Pro  
 2340 2345 2350  
 Gly Gln Glu Phe Leu Ser Lys Ser His Leu Tyr Glu His Leu Thr Leu  
 2355 2360 2365  
 55 Glu Lys Ser Ser Ser Asn Leu Ala Val Ser Gly His Pro Phe Tyr Gln  
 2370 2375 2380  
 Val Ser Ala Thr Arg Asn Glu Lys Met Arg His Leu Ile Thr Thr Gly  
 2385 2390 2395 240  
 Arg Pro Thr Lys Val Phe Val Pro Pro Phe Lys Thr Lys Ser His Phe  
 2405 2410 2415  
 60 His Arg Val Glu Gln Cys Val Arg Asn Ile Asn Leu Glu Glu Asn Arg  
 2420 2425 2430  
 Gln Lys Gln Asn Ile Asp Gly His Gly Ser Asp Asp Ser Lys Asn Lys

	2435		2440		2445
	Ile Asn Asp Asn Glu	Ile His Gln Phe Asn Lys	Asn Asn Ser Asn Gln		
	2450	2455	2460		
5	Ala Ala Ala Val Thr	Phe Thr Lys Cys Glu	Glu Glu Pro Leu Asp Leu		
	2465	2470	2475	248	
	Ile Thr Ser Leu Gln	Asn Ala Arg Asp	Ile Gln Asp Met Arg	Ile Lys	
	2485	2490	2495		
	Lys Lys Gln Arg Gln	Arg Val Phe Pro	Gln Pro Gly Ser	Leu Tyr Leu	
10	2500	2505	2510		
	Ala Lys Thr Ser Thr	Leu Pro Arg Ile	Ser Leu Lys Ala	Ala Val Gly	
	2515	2520	2525		
	Gly Gln Val Pro Ser	Ala Cys Ser His	Lys Gln Leu Tyr	Thr Tyr Gly	
	2530	2535	2540		
15	Val Ser Lys His Cys	Ile Lys Ile Asn	Ser Lys Asn Ala	Glu Ser Phe	
	2545	2550	2555	256	
	Gln Phe His Thr Glu	Asp Tyr Phe Gly	Lys Glu Ser Leu	Trp Thr Gly	
	2565	2570	2575		
	Lys Gly Ile Gln Leu	Ala Asp Gly Gly	Trp Leu Ile Pro	Ser Asn Asp	
20	2580	2585	2590		
	Gly Lys Ala Gly Lys	Glu Glu Phe Tyr	Arg Ala Leu Cys	Asp Thr Pro	
	2595	2600	2605		
	Gly Val Asp Pro Lys	Leu Ile Ser Arg	Ile Trp Val Tyr	Asn His Tyr	
	2610	2615	2620		
25	Arg Trp Ile Ile Trp	Lys Leu Ala Ala	Met Glu Cys Ala	Phe Pro Lys	
	2625	2630	2635	264	
	Glu Phe Ala Asn Arg	Cys Leu Ser Pro	Glu Arg Val Leu	Leu Gln Leu	
	2645	2650	2655		
	Lys Tyr Arg Tyr Asp	Thr Glu Ile Asp	Arg Ser Arg Arg	Ser Ala Ile	
30	2660	2665	2670		
	Lys Lys Ile Met Glu	Arg Asp Asp Thr	Ala Ala Lys Thr	Leu Val Leu	
	2675	2680	2685		
	Cys Val Ser Asp Ile	Ile Ile Ser Leu	Ser Ala Asn Ile	Ser Glu Thr Ser	
	2690	2695	2700		
35	Ser Asn Lys Thr Ser	Ser Ala Asp Thr	Gln Lys Val Ala	Ile Ile Glu	
	2705	2710	2715	272	
	Leu Thr Asp Gly Trp	Tyr Ala Val Lys	Ala Gln Leu Asp	Pro Pro Leu	
	2725	2730	2735		
	Leu Ala Val Leu Lys	Asn Gly Arg Leu	Thr Val Gly Gln	Lys Ile Ile	
40	2740	2745	2750		
	Leu His Gly Ala Glu	Leu Val Gly Ser	Pro Asp Ala Cys	Thr Pro Leu	
	2755	2760	2765		
	Glu Ala Pro Glu Ser	Leu Met Leu Lys	Ile Ser Ala Asn	Ser Thr Arg	
	2770	2775	2780		
45	Pro Ala Arg Trp Tyr	Thr Lys Leu Gly	Phe Phe Pro Asp	Pro Arg Pro	
	2785	2790	2795	280	
	Phe Pro Leu Pro Leu	Ser Ser Leu Phe	Ser Asp Gly Gly	Asn Val Gly	
	2805	2810	2815		
	Cys Val Asp Val Ile	Ile Ile Gln Arg	Ala Tyr Pro Ile	Gln Trp Met Glu	
50	2820	2825	2830		
	Lys Thr Ser Ser Gly	Leu Tyr Ile Phe	Arg Asn Glu Arg	Glu Glu Glu	
	2835	2840	2845		
	Lys Glu Ala Ala Lys	Tyr Val Glu Ala	Gln Gln Lys Arg	Leu Glu Ala	
	2850	2855	2860		
55	Leu Phe Thr Lys Ile	Gln Glu Glu Phe	Glu Glu His Glu	Glu Asn Thr	
	2865	2870	2875	288	
	Thr Lys Pro Tyr Leu	Pro Ser Arg Ala	Leu Thr Arg Gln	Gln Val Arg	
	2885	2890	2895		
	Ala Leu Gln Asp Gly	Ala Glu Leu Tyr	Glu Ala Val Lys	Asn Ala Ala	
60	2900	2905	2910		
	Asp Pro Ala Tyr Leu	Glu Gly Tyr Phe	Ser Glu Glu Gln	Leu Arg Ala	
	2915	2920	2925		

Leu Asn Asn His Arg Gln Met Leu Asn Asp Lys Lys Gln Ala Gln Ile  
 2930 2935 2940  
 5 Gln Leu Glu Ile Arg Lys Ala Met Glu Ser Ala Glu Gln Lys Glu Gln  
 2945 2950 2955 296  
 Gly Leu Ser Arg Asp Val Thr Thr Val Trp Lys Leu Arg Ile Val Ser  
 2965 2970 2975  
 Tyr Ser Lys Lys Glu Lys Asp Ser Val Ile Leu Ser Ile Trp Arg Pro  
 2980 2985 2990  
 10 Ser Ser Asp Leu Tyr Ser Leu Leu Thr Glu Gly Lys Arg Tyr Arg Ile  
 2995 3000 3005  
 Tyr His Leu Ala Thr Ser Lys Ser Lys Ser Lys Ser Glu Arg Ala Asn  
 3010 3015 3020  
 15 Ile Gln Leu Ala Ala Thr Lys Lys Thr Gln Tyr Gln Gln Leu Pro Val  
 3025 3030 3035 304  
 Ser Asp Glu Ile Leu Phe Gln Ile Tyr Gln Pro Arg Glu Pro Leu His  
 3045 3050 3055  
 Phe Ser Lys Phe Leu Asp Pro Asp Phe Gln Pro Ser Cys Ser Glu Val  
 3060 3065 3070  
 20 Asp Leu Ile Gly Phe Val Val Ser Val Val Lys Lys Thr Gly Leu Ala  
 3075 3080 3085  
 Pro Phe Val Tyr Leu Ser Asp Glu Cys Tyr Asn Leu Leu Ala Ile Lys  
 3090 3095 3100  
 Phe Trp Ile Asp Leu Asn Glu Asp Ile Ile Lys Pro His Met Leu Ile  
 25 3105 3110 3115 312  
 Ala Ala Ser Asn Leu Gln Trp Arg Pro Glu Ser Lys Ser Gly Leu Leu  
 3125 3130 3135  
 Thr Leu Phe Ala Gly Asp Phe Ser Val Phe Ser Ala Ser Pro Lys Glu  
 3140 3145 3150  
 30 Gly His Phe Gln Glu Thr Phe Asn Lys Met Lys Asn Thr Val Glu Asn  
 3155 3160 3165  
 Ile Asp Ile Leu Cys Asn Glu Ala Glu Asn Lys Leu Met His Ile Leu  
 3170 3175 3180  
 His Ala Asn Asp Pro Lys Trp Ser Thr Pro Thr Lys Asp Cys Thr Ser  
 35 3185 3190 3195 320  
 Gly Pro Tyr Thr Ala Gln Ile Ile Pro Gly Thr Gly Asn Lys Leu Leu  
 3205 3210 3215  
 Met Ser Ser Pro Asn Cys Glu Ile Tyr Tyr Gln Ser Pro Leu Ser Leu  
 3220 3225 3230  
 40 Cys Met Ala Lys Arg Lys Ser Val Ser Thr Pro Val Ser Ala Gln Met  
 3235 3240 3245  
 Thr Ser Lys Ser Cys Lys Gly Glu Lys Glu Ile Asp Asp Gln Lys Asn  
 3250 3255 3260  
 Cys Lys Lys Arg Arg Ala Leu Asp Phe Leu Ser Arg Leu Pro Leu Pro  
 45 3265 3270 3275 328  
 Pro Pro Val Ser Pro Ile Cys Thr Phe Val Ser Pro Ala Ala Gln Lys  
 3285 3290 3295  
 Ala Phe Gln Pro Pro Arg Ser Cys Gly Thr Lys Tyr Glu Thr Pro Ile  
 3300 3305 3310  
 50 Lys Lys Lys Glu Leu Asn Ser Pro Gln Met Thr Pro Phe Lys Lys Phe  
 3315 3320 3325  
 Asn Glu Ile Ser Leu Leu Glu Ser Asn Ser Ile Ala Asp Glu Glu Leu  
 3330 3335 3340  
 Ala Leu Ile Asn Thr Gln Ala Leu Leu Ser Gly Ser Thr Gly Glu Lys  
 55 3345 3350 3355 336  
 Gln Phe Ile Ser Val Ser Glu Ser Thr Arg Thr Ala Pro Thr Ser Ser  
 3365 3370 3375  
 Glu Asp Tyr Leu Arg Leu Lys Arg Arg Cys Thr Thr Ser Leu Ile Lys  
 3380 3385 3390  
 60 Glu Gln Glu Ser Ser Gln Ala Ser Thr Glu Glu Cys Glu Lys Asn Lys  
 3395 3400 3405  
 Gln Asp Thr Ile Thr Thr Lys Lys Tyr Ile

3410

3415

## (2) INFORMATION FOR SEQ ID NO:10:

5

## (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 10485 base pairs

(B) TYPE: nucleic acid

10

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

15

(A) NAME/KEY: Coding Sequence

(B) LOCATION: 229...10482

(D) OTHER INFORMATION: BRCA2 (OMI4)

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

20

GGTGGCGCGA GCTTCTGAAA CTAGGCGGCA GAGGCGGAGC CGCTGTGGCA CTGCTGCGCC 60  
 TCTGCTGCGC CTCGGGTGTC TTTTGGGCGG GTGGGTCGCC GCCGGGAGAA GCGTGAGGGG 120  
 ACAGATTTGT GACCGGCGCG GTTTTGTCA GCTTACTCCG GCCAAAAAAG AACTGCACCT 180  
 CTGGAGCGGA CTTATTTACC AAGCATTGGA GGAATATCGT AGGTAAAA ATG CCT ATT 237

25

Met Pro Ile

1

30

GGA TCC AAA GAG AGG CCA ACA TTT TTT GAA ATT TTT AAG ACA CGC TGC 285  
 Gly Ser Lys Glu Arg Pro Thr Phe Phe Glu Ile Phe Lys Thr Arg Cys

35

AAC AAA GCA GAT TTA GGA CCA ATA AGT CTT AAT TGG TTT GAA GAA CTT 333  
 Asn Lys Ala Asp Leu Gly Pro Ile Ser Leu Asn Trp Phe Glu Glu Leu

TCT TCA GAA GCT CCA CCC TAT AAT TCT GAA CCT GCA GAA GAA TCT GAA 381  
 Ser Ser Glu Ala Pro Pro Tyr Asn Ser Glu Pro Ala Glu Glu Ser Glu

40

CAT AAA AAC AAC AAT TAC GAA CCA AAC CTA TTT AAA ACT CCA CAA AGG 429  
 His Lys Asn Asn Asn Tyr Glu Pro Asn Leu Phe Lys Thr Pro Gln Arg

45

AAA CCA TCT TAT AAT CAG CTG GCT TCA ACT CCA ATA ATA TTC AAA GAG 477  
 Lys Pro Ser Tyr Asn Gln Leu Ala Ser Thr Pro Ile Ile Phe Lys Glu

50

CAA GGG CTG ACT CTG CCG CTG TAC CAA TCT CCT GTA AAA GAA TTA GAT 525  
 Gln Gly Leu Thr Leu Pro Leu Tyr Gln Ser Pro Val Lys Glu Leu Asp

55

AAA TTC AAA TTA GAC TTA GGA AGG AAT GTT CCC AAT AGT AGA CAT AAA 573  
 Lys Phe Lys Leu Asp Leu Gly Arg Asn Val Pro Asn Ser Arg His Lys

AGT CTT CGC ACA GTG AAA ACT AAA ATG GAT CAA GCA GAT GAT GTT TCC 621  
 Ser Leu Arg Thr Val Lys Thr Lys Met Asp Gln Ala Asp Asp Val Ser

60

TGT CCA CTT CTA AAT TCT TGT CTT AGT GAA AGT CCT GTT GTT CTA CAA 669  
 Cys Pro Leu Leu Asn Ser Cys Leu Ser Glu Ser Pro Val Val Leu Gln

5	TGT ACA CAT GTA ACA CCA CAA AGA GAT AAG TCA GTG GTA TGT GGG AGT Cys Thr His Val Thr Pro Gln Arg Asp Lys Ser Val Val Cys Gly Ser	717
	150 155 160	
10	TTG TTT CAT ACA CCA AAG TTT GTG AAG GGT CGT CAG ACA CCA AAA CAT Leu Phe His Thr Pro Lys Phe Val Lys Gly Arg Gln Thr Pro Lys His	765
	165 170 175	
15	ATT TCT GAA AGT CTA GGA GCT GAG GTG GAT CCT GAT ATG TCT TGG TCA Ile Ser Glu Ser Leu Gly Ala Glu Val Asp Pro Asp Met Ser Trp Ser	813
	180 185 190 195	
20	AGT TCT TTA GCT ACA CCA CCC ACC CTT AGT TCT ACT GTG CTC ATA GTC Ser Ser Leu Ala Thr Pro Pro Thr Leu Ser Ser Thr Val Leu Ile Val	861
	200 205 210	
25	AGA AAT GAA GAA GCA TCT GAA ACT GTA TTT CCT CAT GAT ACT ACT GCT Arg Asn Glu Glu Ala Ser Glu Thr Val Phe Pro His Asp Thr Thr Ala	909
	215 220 225	
30	AAT GTG AAA AGC TAT TTT TCC AAT CAT GAT GAA AGT CTG AAG AAA AAT Asn Val Lys Ser Tyr Phe Ser Asn His Asp Glu Ser Leu Lys Lys Asn	957
	230 235 240	
35	GAT AGA TTT ATC GCT TCT GTG ACA GAC AGT GAA AAC ACA AAT CAA AGA Asp Arg Phe Ile Ala Ser Val Thr Asp Ser Glu Asn Thr Asn Gln Arg	1005
	245 250 255	
40	GAA GCT GCA AGT CAT GGA TTT GGA AAA ACA TCA GGG AAT TCA TTT AAA Glu Ala Ala Ser His Gly Phe Gly Lys Thr Ser Gly Asn Ser Phe Lys	1053
	260 265 270 275	
45	GTA AAT AGC TGC AAA GAC CAC ATT GGA AAG TCA ATG CCA AAT GTC CTA Val Asn Ser Cys Lys Asp His Ile Gly Lys Ser Met Pro Asn Val Leu	1101
	280 285 290	
50	GAA GAT GAA GTA TAT GAA ACA GTT GTA GAT ACC TCT GAA GAA GAT AGT Glu Asp Glu Val Tyr Glu Thr Val Val Asp Thr Ser Glu Glu Asp Ser	1149
	295 300 305	
55	TTT TCA TTA TGT TTT TCT AAA TGT AGA ACA AAA AAT CTA CAA AAA GTA Phe Ser Leu Cys Phe Ser Lys Cys Arg Thr Lys Asn Leu Gln Lys Val	1197
	310 315 320	
60	AGA ACT AGC AAG ACT AGG AAA AAA ATT TTC CAT GAA GCA AAC GCT GAT Arg Thr Ser Lys Thr Arg Lys Lys Ile Phe His Glu Ala Asn Ala Asp	1245
	325 330 335	
65	GAA TGT GAA AAA TCT AAA AAC CAA GTG AAA GAA AAA TAC TCA TTT GTA Glu Cys Glu Lys Ser Lys Asn Gln Val Lys Glu Lys Tyr Ser Phe Val	1293
	340 345 350 355	
70	TCT GAA GTG GAA CCA AAT GAT ACT GAT CCA TTA GAT TCA AAT GTA GCA Ser Glu Val Glu Pro Asn Asp Thr Asp Pro Leu Asp Ser Asn Val Ala	1341
	360 365 370	
75	CAT CAG AAG CCC TTT GAG AGT GGA AGT GAC AAA ATC TCC AAG GAA GTT His Gln Lys Pro Phe Glu Ser Gly Ser Asp Lys Ile Ser Lys Glu Val	1389
	375 380 385	

	GTA CCG TCT TTG GCC TGT GAA TGG TCT CAA CTA ACC CTT TCA GGT CTA	1437
	Val Pro Ser Leu Ala Cys Glu Trp Ser Gln Leu Thr Leu Ser Gly Leu	
	390 395 400	
5	AAT GGA GCC CAG ATG GAG AAA ATA CCC CTA TTG CAT ATT TCT TCA TGT	1485
	Asn Gly Ala Gln Met Glu Lys Ile Pro Leu Leu His Ile Ser Ser Cys	
	405 410 415	
10	GAC CAA AAT ATT TCA GAA AAA GAC CTA TTA GAC ACA GAG AAC AAA AGA	1533
	Asp Gln Asn Ile Ser Glu Lys Asp Leu Leu Asp Thr Glu Asn Lys Arg	
	420 425 430 435	
15	AAG AAA GAT TTT CTT ACT TCA GAG AAT TCT TTG CCA CGT ATT TCT AGC	1581
	Lys Lys Asp Phe Leu Thr Ser Glu Asn Ser Leu Pro Arg Ile Ser Ser	
	440 445 450	
20	CTA CCA AAA TCA GAG AAG CCA TTA AAT GAG GAA ACA GTG GTA AAT AAG	1629
	Leu Pro Lys Ser Glu Lys Pro Leu Asn Glu Glu Thr Val Val Asn Lys	
	455 460 465	
25	AGA GAT GAA GAG CAG CAT CTT GAA TCT CAT ACA GAC TGC ATT CTT GCA	1677
	Arg Asp Glu Glu Gln His Leu Glu Ser His Thr Asp Cys Ile Leu Ala	
	470 475 480	
30	GTA AAG CAG GCA ATA TCT GGA ACT TCT CCA GTG GCT TCT TCA TTT CAG	1725
	Val Lys Gln Ala Ile Ser Gly Thr Ser Pro Val Ala Ser Ser Phe Gln	
	485 490 495	
35	GGT ATC AAA AAG TCT ATA TTC AGA ATA AGA GAA TCA CCT AAA GAG ACT	1773
	Gly Ile Lys Lys Ser Ile Phe Arg Ile Arg Glu Ser Pro Lys Glu Thr	
	500 505 510 515	
40	TTC AAT GCA AGT TTT TCA GGT CAT ATG ACT GAT CCA AAC TTT AAA AAA	1821
	Phe Asn Ala Ser Phe Ser Gly His Met Thr Asp Pro Asn Phe Lys Lys	
	520 525 530	
45	GAA ACT GAA GCC TCT GAA AGT GGA CTG GAA ATA CAT ACT GTT TGC TCA	1869
	Glu Thr Glu Ala Ser Glu Ser Gly Leu Glu Ile His Thr Val Cys Ser	
	535 540 545	
50	CAG AAG GAG GAC TCC TTA TGT CCA AAT TTA ATT GAT AAT GGA AGC TGG	1917
	Gln Lys Glu Asp Ser Leu Cys Pro Asn Leu Ile Asp Asn Gly Ser Trp	
	550 555 560	
55	CCA GCC ACC ACC ACA CAG AAT TCT GTA GCT TTG AAG AAT GCA GGT TTA	1965
	Pro Ala Thr Thr Thr Gln Asn Ser Val Ala Leu Lys Asn Ala Gly Leu	
	565 570 575	
60	ATA TCC ACT TTG AAA AAG AAA ACA AAT AAG TTT ATT TAT GCT ATA CAT	2013
	Ile Ser Thr Leu Lys Lys Lys Thr Asn Lys Phe Ile Tyr Ala Ile His	
	580 585 590 595	
65	GAT GAA ACA TCT TAT AAA GGA AAA AAA ATA CCG AAA GAC CAA AAA TCA	2061
	Asp Glu Thr Ser Tyr Lys Gly Lys Lys Ile Pro Lys Asp Gln Lys Ser	
	600 605 610	
70	GAA CTA ATT AAC TGT TCA GCC CAG TTT GAA GCA AAT GCT TTT GAA GCA	2109
	Glu Leu Ile Asn Cys Ser Ala Gln Phe Glu Ala Asn Ala Phe Glu Ala	
	615 620 625	
75	CCA CTT ACA TTT GCA AAT GCT GAT TCA GGT TTA TTG CAT TCT TCT GTG	2157





	870	875	880	
5	TCA GAC AAT GAG AAT AAT TTT Ser Asp Asn Glu Asn Asn Phe 885	GTC TTC CAA GTA GCT AAT GAA AGG AAT Val Phe Gln Val Ala Asn Glu Arg Asn 890		2925
10	AAT CTT GCT TTA GGA AAT ACT AAG GAA CTT CAT GAA ACA GAC TTG ACT Asn Leu Ala Leu Gly Asn Thr Lys Glu Leu His Glu Thr Asp Leu Thr 900		910	2973
15	TGT GTA AAC GAA CCC ATT TTC AAG AAC TCT ACC ATG GTT TTA TAT GGA Cys Val Asn Glu Pro Ile Phe Lys Asn Ser Thr Met Val Leu Tyr Gly 920		925	3021
20	GAC ACA GGT GAT AAA CAA GCA ACC CAA GTG TCA ATT AAA AAA GAT TTG Asp Thr Gly Asp Lys Gln Ala Thr Gln Val Ser Ile Lys Lys Asp Leu 935		940	3069
25	GTT TAT GTT CTT GCA GAG GAG AAC AAA AAT AGT GTA AAG CAG CAT ATA Val Tyr Val Leu Ala Glu Glu Asn Lys Asn Ser Val Lys Gln His Ile 950		955	3117
30	AAA ATG ACT CTA GGT CAA GAT TTA AAA TCG GAC ATC TCC TTG AAT ATA Lys Met Thr Leu Gly Gln Asp Leu Lys Ser Asp Ile Ser Leu Asn Ile 965		970	3165
35	GAT AAA ATA CCA GAA AAA AAT AAT GAT TAC ATG AAC AAA TGG GCA GGA Asp Lys Ile Pro Glu Lys Asn Asn Asp Tyr Met Asn Lys Trp Ala Gly 980		985	3213
40	CTC TTA GGT CCA ATT TCA AAT CAC AGT TTT GGA GGT AGC TTC AGA ACA Leu Leu Gly Pro Ile Ser Asn His Ser Phe Gly Gly Ser Phe Arg Thr 1000		1005	3261
45	GCT TCA AAT AAG GAA ATC AAG CTC TCT GAA CAT AAC ATT AAG AAG AGC Ala Ser Asn Lys Glu Ile Lys Leu Ser Glu His Asn Ile Lys Lys Ser 1015		1020	3309
50	AAA ATG TTC TTC AAA GAT ATT GAA GAA CAA TAT CCT ACT AGT TTA GCT Lys Met Phe Phe Lys Asp Ile Glu Glu Gln Tyr Pro Thr Ser Leu Ala 1030		1035	3357
55	TGT GTT GAA ATT GTA AAT ACC TTG GCA TTA GAT AAT CAA AAG AAA CTG Cys Val Glu Ile Val Asn Thr Leu Ala Leu Asp Asn Gln Lys Lys Leu 1045		1050	3405
60	AGC AAG CCT CAG TCA ATT AAT ACT GTA TCT GCA CAT TTA CAG AGT AGT Ser Lys Pro Gln Ser Ile Asn Thr Val Ser Ala His Leu Gln Ser Ser 1060		1065	3453
	GTA GTT GTT TCT GAT TGT AAA AAT AGT CAT ATA ACC CCT CAG ATG TTA Val Val Val Ser Asp Cys Lys Asn Ser His Ile Thr Pro Gln Met Leu 1080		1085	3501
	TTT TCC AAG CAG GAT TTT AAT TCA AAC CAT AAT TTA ACA CCT AGC CAA Phe Ser Lys Gln Asp Phe Asn Ser Asn His Asn Leu Thr Pro Ser Gln 1095		1100	3549
	AAG GCA GAA ATT ACA GAA CTT TCT ACT ATA TTA GAA GAA TCA GGA AGT Lys Ala Glu Ile Thr Glu Leu Ser Thr Ile Leu Glu Glu Ser Gly Ser 1110		1115	3597

5	CAG TTT GAA TTT ACT CAG TTT AGA AAG CCA AGC TAC ATA TTG CAG AAG Gln Phe Glu Phe Thr Gln Phe Arg Lys Pro Ser Tyr Ile Leu Gln Lys 1125 1130 1135	3645
10	AGT ACA TTT GAA GTG CCT GAA AAC CAG ATG ACT ATC TTA AAG ACC ACT Ser Thr Phe Glu Val Pro Glu Asn Gln Met Thr Ile Leu Lys Thr Thr 1140 1145 1150 1155	3693
15	TCT GAG GAA TGC AGA GAT GCT GAT CTT CAT GTC ATA ATG AAT GCC CCA Ser Glu Glu Cys Arg Asp Ala Asp Leu His Val Ile Met Asn Ala Pro 1160 1165 1170	3741
20	TCG ATT GGT CAG GTA GAC AGC AGC AAG CAA TTT GAA GGT ACA GTT GAA Ser Ile Gly Gln Val Asp Ser Ser Lys Gln Phe Glu Gly Thr Val Glu 1175 1180 1185	3789
25	ATT AAA CGG AAG TTT GCT GGC CTG TTG AAA ATT GAC TGT AAC AAA AGT Ile Lys Arg Lys Phe Ala Gly Leu Leu Lys Asn Asp Cys Asn Lys Ser 1190 1195 1200	3837
30	GCT TCT GGT TAT TTA ACA GAT GAA AAT GAA GTG GGG TTT AGG GGC TTT Ala Ser Gly Tyr Leu Thr Asp Glu Asn Glu Val Gly Phe Arg Gly Phe 1205 1210 1215	3885
35	TAT TCT GCT CAT GGC ACA AAA CTG AAT GTT TCT ACT GAA GCT CTG CAA Tyr Ser Ala His Gly Thr Lys Leu Asn Val Ser Thr Glu Ala Leu Gln 1220 1225 1230 1235	3933
40	AAA GCT GTG AAA CTG TTT AGT GAT ATT GAG AAT ATT AGT GAG GAA ACT Lys Ala Val Lys Leu Phe Ser Asp Ile Glu Asn Ile Ser Glu Glu Thr 1240 1245 1250	3981
45	TCT GCA GAG GTA CAT CCA ATA AGT TTA TCT TCA AGT AAA TGT CAT GAT Ser Ala Glu Val His Pro Ile Ser Leu Ser Ser Ser Lys Cys His Asp 1255 1260 1265	4029
50	TCT GTT GTT TCA ATG TTT AAG ATA GAA AAT CAT AAT GAT AAA ACT GTA Ser Val Val Ser Met Phe Lys Ile Glu Asn His Asn Asp Lys Thr Val 1270 1275 1280	4077
55	AGT GAA AAA AAT AAT AAA TGC CAA CTG ATA TTA CAA AAT AAT ATT GAA Ser Glu Lys Asn Asn Lys Cys Gln Leu Ile Leu Gln Asn Asn Ile Glu 1285 1290 1295	4125
60	ATG ACT ACT GGC ACT TTT GTT GAA GAA ATT ACT GAA AAT TAC AAG AGA Met Thr Thr Gly Thr Phe Val Glu Glu Ile Thr Glu Asn Tyr Lys Arg 1300 1305 1310 1315	4173
65	AAT ACT GAA AAT GAA GAT AAC AAA TAT ACT GCT GCC AGT AGA AAT TCT Asn Thr Glu Asn Glu Asp Asn Lys Tyr Thr Ala Ala Ser Arg Asn Ser 1320 1325 1330	4221
70	CAT AAC TTA GAA TTT GAT GGC AGT GAT TCA AGT AAA AAT GAT ACT GTT His Asn Leu Glu Phe Asp Gly Ser Asp Ser Ser Lys Asn Asp Thr Val 1335 1340 1345	4269
75	TGT ATT CAT AAA GAT GAA ACG GAC TTG CTA TTT ACT GAT CAG CAC AAC Cys Ile His Lys Asp Glu Thr Asp Leu Leu Phe Thr Asp Gln His Asn 1350 1355 1360	4317

	ATA TGT CTT AAA TTA TCT GGC CAG TTT ATG AAG GAG GGA AAC ACT CAG Ile Cys Leu Lys Leu Ser Gly Gln Phe Met Lys Glu Gly Asn Thr Gln 1365 1370 1375	4365
5	ATT AAA GAA GAT TTG TCA GAT TTA ACT TTT TTG GAA GTT GCG AAA GCT Ile Lys Glu Asp Leu Ser Asp Leu Thr Phe Leu Glu Val Ala Lys Ala 1380 1385 1390 1395	4413
10	CAA GAA GCA TGT CAT GGT AAT ACT TCA AAT AAA GAA CAG TTA ACT GCT Gln Glu Ala Cys His Gly Asn Thr Ser Asn Lys Glu Gln Leu Thr Ala 1400 1405 1410	4461
15	ACT AAA ACG GAG CAA AAT ATA AAA GAT TTT GAG ACT TCT GAT ACA TTT Thr Lys Thr Glu Gln Asn Ile Lys Asp Phe Glu Thr Ser Asp Thr Phe 1415 1420 1425	4509
20	TTT CAG ACT GCA AGT GGG AAA AAT ATT AGT GTC GCC AAA GAG TCA TTT Phe Gln Thr Ala Ser Gly Lys Asn Ile Ser Val Ala Lys Glu Ser Phe 1430 1435 1440	4557
25	AAT AAA ATT GTA AAT TTC TTT GAT CAG AAA CCA GAA GAA TTG CAT AAC Asn Lys Ile Val Asn Phe Phe Asp Gln Lys Pro Glu Glu Leu His Asn 1445 1450 1455	4605
	TTT TCC TTA AAT TCT GAA TTA CAT TCT GAC ATA AGA AAG AAC AAA ATG Phe Ser Leu Asn Ser Glu Leu His Ser Asp Ile Arg Lys Asn Lys Met 1460 1465 1470 1475	4653
30	GAC ATT CTA AGT TAT GAG GAA ACA GAC ATA GTT AAA CAC AAA ATA CTG Asp Ile Leu Ser Tyr Glu Glu Thr Asp Ile Val Lys His Lys Ile Leu 1480 1485 1490	4701
35	AAA GAA AGT GTC CCA GTT GGT ACT GGA AAT CAA CTA GTG ACC TTC CAG Lys Glu Ser Val Pro Val Gly Thr Gly Asn Gln Leu Val Thr Phe Gln 1495 1500 1505	4749
40	GGA CAA CCC GAA CGT GAT GAA AAG ATC AAA GAA CCT ACT CTG TTG GGT Gly Gln Pro Glu Arg Asp Glu Lys Ile Lys Glu Pro Thr Leu Leu Gly 1510 1515 1520	4797
45	TTT CAT ACA GCT AGC GGG AAA AAA GTT AAA ATT GCA AAG GAA TCT TTG Phe His Thr Ala Ser Gly Lys Lys Val Lys Ile Ala Lys Glu Ser Leu 1525 1530 1535	4845
	GAC AAA GTG AAA AAC CTT TTT GAT GAA AAA GAG CAA GGT ACT AGT GAA Asp Lys Val Lys Asn Leu Phe Asp Glu Lys Glu Gln Gly Thr Ser Glu 1540 1545 1550 1555	4893
50	ATC ACC AGT TTT AGC CAT CAA TGG GCA AAG ACC CTA AAG TAC AGA GAG Ile Thr Ser Phe Ser His Gln Trp Ala Lys Thr Leu Lys Tyr Arg Glu 1560 1565 1570	4941
55	GCC TGT AAA GAC CTT GAA TTA GCA TGT GAG ACC ATT GAG ATC ACA GCT Ala Cys Lys Asp Leu Glu Leu Ala Cys Glu Thr Ile Glu Ile Thr Ala 1575 1580 1585	4989
60	GCC CCA AAG TGT AAA GAA ATG CAG AAT TCT CTC AAT AAT GAT AAA AAC Ala Pro Lys Cys Lys Glu Met Gln Asn Ser Leu Asn Asn Asp Lys Asn 1590 1595 1600	5037
	CTT GTT TCT ATT GAG ACT GTG GTG CCA CCT AAG CTC TTA AGT GAT AAT	5085

	Leu Val Ser Ile Glu Thr Val Val Pro Pro Lys Leu Leu Ser Asp Asn	
	1605 1610 1615	
5	TTA TGT AGA CAA ACT GAA AAT CTC AAA ACA TCA AAA AGT ATC TTT TTG Leu Cys Arg Gln Thr Glu Asn Leu Lys Thr Ser Lys Ser Ile Phe Leu	5133
	1620 1625 1630 1635	
10	AAA GTT AAA GTA CAT GAA AAT GTA GAA AAA GAA ACA GCA AAA AGT CCT Lys Val Lys Val His Glu Asn Val Glu Lys Glu Thr Ala Lys Ser Pro	5181
	1640 1645 1650	
15	GCA ACT TGT TAC ACA AAT CAG TCC CCT TAT TCA GTC ATT GAA AAT TCA Ala Thr Cys Tyr Thr Asn Gln Ser Pro Tyr Ser Val Ile Glu Asn Ser	5229
	1655 1660 1665	
20	GCC TTA GCT TTT TAC ACA AGT TGT AGT AGA AAA ACT TCT GTG AGT CAG Ala Leu Ala Phe Tyr Thr Ser Cys Ser Arg Lys Thr Ser Val Ser Gln	5277
	1670 1675 1680	
25	ACT TCA TTA CTT GAA GCA AAA AAA TGG CTT AGA GAA GGA ATA TTT GAT Thr Ser Leu Leu Glu Ala Lys Lys Trp Leu Arg Glu Gly Ile Phe Asp	5325
	1685 1690 1695	
30	GGT CAA CCA GAA AGA ATA AAT ACT GCA GAT TAT GTA GGA AAT TAT TTG Gly Gln Pro Glu Arg Ile Asn Thr Ala Asp Tyr Val Gly Asn Tyr Leu	5373
	1700 1705 1710 1715	
35	TAT GAA AAT AAT TCA AAC AGT ACT ATA GCT GAA AAT GAC AAA AAT CAT Tyr Glu Asn Asn Ser Asn Ser Thr Ile Ala Glu Asn Asp Lys Asn His	5421
	1720 1725 1730	
40	CTC TCC GAA AAA CAA GAT ACT TAT TTA AGT AAC AGT AGC ATG TCT AAC Leu Ser Glu Lys Gln Asp Thr Tyr Leu Ser Asn Ser Ser Met Ser Asn	5469
	1735 1740 1745	
45	AGC TAT TCC TAC CAT TCT GAT GAG GTA TAT AAT GAT TCA GGA TAT CTC Ser Tyr Ser Tyr His Ser Asp Glu Val Tyr Asn Asp Ser Gly Tyr Leu	5517
	1750 1755 1760	
50	TCA AAA AAT AAA CTT GAT TCT GGT ATT GAG CCA GTA TTG AAG AAT GTT Ser Lys Asn Lys Leu Asp Ser Gly Ile Glu Pro Val Leu Lys Asn Val	5565
	1765 1770 1775	
55	GAA GAT CAA AAA AAC ACT AGT TTT TCC AAA GTA ATA TCC AAT GTA AAA Glu Asp Gln Lys Asn Thr Ser Phe Ser Lys Val Ile Ser Asn Val Lys	5613
	1780 1785 1790 1795	
60	GAT GCA AAT GCA TAC CCA CAA ACT GTA AAT GAA GAT ATT TGC GTT GAG Asp Ala Asn Ala Tyr Pro Gln Thr Val Asn Glu Asp Ile Cys Val Glu	5661
	1800 1805 1810	
65	GAA CTT GTG ACT AGC TCT TCA CCC TGC AAA AAT AAA AAT GCA GCC ATT Glu Leu Val Thr Ser Ser Ser Pro Cys Lys Asn Lys Asn Ala Ala Ile	5709
	1815 1820 1825	
70	AAA TTG TCC ATA TCT AAT AGT AAT AAT TTT GAG GTA GGG CCA CCT GCA Lys Leu Ser Ile Ser Asn Ser Asn Asn Phe Glu Val Gly Pro Pro Ala	5757
	1830 1835 1840	
75	TTT AGG ATA GCC AGT GGT AAA ATC GTT TGT GTT TCA CAT GAA ACA ATT Phe Arg Ile Ala Ser Gly Lys Ile Val Cys Val Ser His Glu Thr Ile	5805

	1845	1850	1855	
5	AAA AAA GTG AAA GAC ATA TTT ACA GAC AGT TTC AGT AAA GTA ATT AAG Lys Lys Val Lys Asp Ile Phe Thr Asp Ser Phe Ser Lys Val Ile Lys 1860 1865 1870 1875	5853		
10	GAA AAC AAC GAG AAT AAA TCA AAA ATT TGC CAA ACG AAA ATT ATG GCA Glu Asn Asn Glu Asn Lys Ser Lys Ile Cys Gln Thr Lys Ile Met Ala 1880 1885 1890	5901		
15	GGT TGT TAC GAG GCA TTG GAT GAT TCA GAG GAT ATT CTT CAT AAC TCT Gly Cys Tyr Glu Ala Leu Asp Asp Ser Glu Asp Ile Leu His Asn Ser 1895 1900 1905	5949		
20	CTA GAT AAT GAT GAA TGT AGC ACG CAT TCA CAT AAG GTT TTT GCT GAC Leu Asp Asn Asp Glu Cys Ser Thr His Ser His Lys Val Phe Ala Asp 1910 1915 1920	5997		
25	ATT CAG AGT GAA GAA ATT TTA CAA CAT AAC CAA AAT ATG TCT GGA TTG Ile Gln Ser Glu Glu Ile Leu Gln His Asn Gln Asn Met Ser Gly Leu 1925 1930 1935	6045		
30	GAG AAA GTT TCT AAA ATA TCA CCT TGT GAT GTT AGT TTG GAA ACT TCA Glu Lys Val Ser Lys Ile Ser Pro Cys Asp Val Ser Leu Glu Thr Ser 1940 1945 1950 1955	6093		
35	GAT ATA TGT AAA TGT AGT ATA GGG AAG CTT CAT AAG TCA GTC TCA TCT Asp Ile Cys Lys Cys Ser Ile Gly Lys Leu His Lys Ser Val Ser Ser 1960 1965 1970	6141		
40	GCA AAT ACT TGT GGG ATT TTT AGC ACA GCA AGT GGA AAA TCT GTC CAG Ala Asn Thr Cys Gly Ile Phe Ser Thr Ala Ser Gly Lys Ser Val Gln 1975 1980 1985	6189		
45	GTA TCA GAT GCT TCA TTA CAA AAC GCA AGA CAA GTG TTT TCT GAA ATA Val Ser Asp Ala Ser Leu Gln Asn Ala Arg Gln Val Phe Ser Glu Ile 1990 1995 2000	6237		
50	GAA GAT AGT ACC AAG CAA GTC TTT TCC AAA GTA TTG TTT AAA AGT AAC Glu Asp Ser Thr Lys Gln Val Phe Ser Lys Val Leu Phe Lys Ser Asn 2005 2010 2015	6285		
55	GAA CAT TCA GAC CAG CTC ACA AGA GAA GAA AAT ACT GCT ATA CGT ACT Glu His Ser Asp Gln Leu Thr Arg Glu Glu Asn Thr Ala Ile Arg Thr 2020 2025 2030 2035	6333		
60	CCA GAA CAT TTA ATA TCC CAA AAA GGC TTT TCA TAT AAT GTG GTA AAT Pro Glu His Leu Ile Ser Gln Lys Gly Phe Ser Tyr Asn Val Val Asn 2040 2045 2050	6381		
65	TCA TCT GCT TTC TCT GGA TTT AGT ACA GCA AGT GGA AAG CAA GTT TCC Ser Ser Ala Phe Ser Gly Phe Ser Thr Ala Ser Gly Lys Gln Val Ser 2055 2060 2065	6429		
70	ATT TTA GAA AGT TCC TTA CAC AAA GTT AAG GGA GTG TTA GAG GAA TTT Ile Leu Glu Ser Ser Leu His Lys Val Lys Gly Val Leu Glu Glu Phe 2070 2075 2080	6477		
75	GAT TTA ATC AGA ACT GAG CAT AGT CTT CAC TAT TCA CCT ACG TCT AGA Asp Leu Ile Arg Thr Glu His Ser Leu His Tyr Ser Pro Thr Ser Arg 2085 2090 2095	6525		

5	CAA AAT GTA TCA AAA ATA CTT CCT CGT GTT GAT AAG AGA AAC CCA GAG Gln Asn Val Ser Lys Ile Leu Pro Arg Val Asp Lys Arg Asn Pro Glu 2100 2105 2110 2115	6573
10	CAC TGT GTA AAC TCA GAA ATG GAA AAA ACC TGC AGT AAA GAA TTT AAA His Cys Val Asn Ser Glu Met Glu Lys Thr Cys Ser Lys Glu Phe Lys 2120 2125 2130	6621
15	TTA TCA AAT AAC TTA AAT GTT GAA GGT GGT TCT TCA GAA AAT AAT CAC Leu Ser Asn Asn Leu Asn Val Glu Gly Gly Ser Ser Glu Asn Asn His 2135 2140 2145	6669
20	TCT ATT AAA GTT TCT CCA TAT CTC TCT CAA TTT CAA CAA GAC AAA CAA Ser Ile Lys Val Ser Pro Tyr Leu Ser Gln Phe Gln Gln Asp Lys Gln 2150 2155 2160	6717
25	CAG TTG GTA TTA GGA ACC AAA GTC TCA CTT GTT GAG AAC ATT CAT GTT Gln Leu Val Leu Gly Thr Lys Val Ser Leu Val Glu Asn Ile His Val 2165 2170 2175	6765
30	TTG GGA AAA GAA CAG GCT TCA CCT AAA AAC GTA AAA ATG GAA ATT GGT Leu Gly Lys Glu Gln Ala Ser Pro Lys Asn Val Lys Met Glu Ile Gly 2180 2185 2190 2195	6813
35	AAA ACT GAA ACT TTT TCT GAT GTT CCT GTG AAA ACA AAT ATA GAA GTT Lys Thr Glu Thr Phe Ser Asp Val Pro Val Lys Thr Asn Ile Glu Val 2200 2205 2210	6861
40	TGT TCT ACT TAC TCC AAA GAT TCA GAA AAC TAC TTT GAA ACA GAA GCA Cys Ser Thr Tyr Ser Lys Asp Ser Glu Asn Tyr Phe Glu Thr Glu Ala 2215 2220 2225	6909
45	GTA GAA ATT GCT AAA GCT TTT ATG GAA GAT GAT GAA CTG ACA GAT TCT Val Glu Ile Ala Lys Ala Phe Met Glu Asp Asp Glu Leu Thr Asp Ser 2230 2235 2240	6957
50	AAA CTG CCA AGT CAT GCC ACA CAT TCT CTT TTT ACA TGT CCC GAA AAT Lys Leu Pro Ser His Ala Thr His Ser Leu Phe Thr Cys Pro Glu Asn 2245 2250 2255	7005
55	GAG GAA ATG GTT TTG TCA AAT TCA AGA ATT GGA AAA AGA AGA GGA GAG Glu Glu Met Val Leu Ser Asn Ser Arg Ile Gly Lys Arg Arg Gly Glu 2260 2265 2270 2275	7053
60	CCC CTT ATC TTA GTG GGA GAA CCC TCA ATC AAA AGA AAC TTA TTA AAT Pro Leu Ile Leu Val Gly Glu Pro Ser Ile Lys Arg Asn Leu Leu Asn 2280 2285 2290	7101
65	GAA TTT GAC AGG ATA ATA GAA AAT CAA GAA AAA TCC TTA AAG GCT TCA Glu Phe Asp Arg Ile Ile Glu Asn Gln Glu Lys Ser Leu Lys Ala Ser 2295 2300 2305	7149
70	AAA AGC ACT CCA GAT GGC ACA ATA AAA GAT CGA AGA TTG TTT ATG CAT Lys Ser Thr Pro Asp Gly Thr Ile Lys Asp Arg Arg Leu Phe Met His 2310 2315 2320	7197
75	CAT GTT TCT TTA GAG CCG ATT ACC TGT GTA CCC TTT CGC ACA ACT AAG His Val Ser Leu Glu Pro Ile Thr Cys Val Pro Phe Arg Thr Thr Lys 2325 2330 2335	7245

	GAA CGT CAA GAG ATA CAG AAT CCA AAT TTT ACC GCA CCT GGT CAA GAA Glu Arg Gln Glu Ile Gln Asn Pro Asn Phe Thr Ala Pro Gly Gln Glu 2340 2345 2350 2355	7293
5	TTT CTG TCT AAA TCT CAT TTG TAT GAA CAT CTG ACT TTG GAA AAA TCT Phe Leu Ser Lys Ser His Leu Tyr Glu His Leu Thr Leu Glu Lys Ser 2360 2365 2370	7341
10	TCA AGC AAT TTA GCA GTT TCA GGA CAT CCA TTT TAT CAA GTT TCT GCT Ser Ser Asn Leu Ala Val Ser Gly His Pro Phe Tyr Gln Val Ser Ala 2375 2380 2385	7389
15	ACA AGA AAT GAA AAA ATG AGA CAC TTG ATT ACT ACA GGC AGA CCA ACC Thr Arg Asn Glu Lys Met Arg His Leu Ile Thr Thr Gly Arg Pro Thr 2390 2395 2400	7437
20	AAA GTC TTT GTT CCA CCT TTT AAA ACT AAA TCG CAT TTT CAC AGA GTT Lys Val Phe Val Pro Pro Phe Lys Thr Lys Ser His Phe His Arg Val 2405 2410 2415	7485
25	GAA CAG TGT GTT AGG AAT ATT AAC TTG GAG GAA AAC AGA CAA AAG CAA Glu Gln Cys Val Arg Asn Ile Asn Leu Glu Glu Asn Arg Gln Lys Gln 2420 2425 2430 2435	7533
	AAC ATT GAT GGA CAT GGC TCT GAT GAT AGT AAA AAT AAG ATT AAT GAC Asn Ile Asp Gly His Gly Ser Asp Asp Ser Lys Asn Lys Ile Asn Asp 2440 2445 2450	7581
30	AAT GAG ATT CAT CAG TTT AAC AAA AAC AAC TCC AAT CAA GCA GCA GCT Asn Glu Ile His Gln Phe Asn Lys Asn Asn Ser Asn Gln Ala Ala Ala 2455 2460 2465	7629
35	GTA ACT TTC ACA AAG TGT GAA GAA GAA CCT TTA GAT TTA ATT ACA AGT Val Thr Phe Thr Lys Cys Glu Glu Glu Pro Leu Asp Leu Ile Thr Ser 2470 2475 2480	7677
40	CTT CAG AAT GCC AGA GAT ATA CAG GAT ATG CGA ATT AAG AAG AAA CAA Leu Gln Asn Ala Arg Asp Ile Gln Asp Met Arg Ile Lys Lys Lys Gln 2485 2490 2495	7725
45	AGG CAA CGC GTC TTT CCA CAG CCA GGC AGT CTG TAT CTT GCA AAA ACA Arg Gln Arg Val Phe Pro Gln Pro Gly Ser Leu Tyr Leu Ala Lys Thr 2500 2505 2510 2515	7773
	TCC ACT CTG CCT CGA ATC TCT CTG AAA GCA GCA GTA GGA GGC CAA GTT Ser Thr Leu Pro Arg Ile Ser Leu Lys Ala Ala Val Gly Gly Gln Val 2520 2525 2530	7821
50	CCC TCT GCG TGT TCT CAT AAA CAG CTG TAT ACG TAT GGC GTT TCT AAA Pro Ser Ala Cys Ser His Lys Gln Leu Tyr Thr Tyr Gly Val Ser Lys 2535 2540 2545	7869
55	CAT TGC ATA AAA ATT AAC AGC AAA AAT GCA GAG TCT TTT CAG TTT CAC His Cys Ile Lys Ile Asn Ser Lys Asn Ala Glu Ser Phe Gln Phe His 2550 2555 2560	7917
60	ACT GAA GAT TAT TTT GGT AAG GAA AGT TTA TGG ACT GGA AAA GGA ATA Thr Glu Asp Tyr Phe Gly Lys Glu Ser Leu Trp Thr Gly Lys Gly Ile 2565 2570 2575	7965
	CAG TTG GCT GAT GGT GGA TGG CTC ATA CCC TCC AAT GAT GGA AAG GCT	8013

130



	2820	2825	2830	2835	
5	TCT GGA TTA TAC ATA TTT CGC AAT GAA AGA GAG GAA GAA AAG GAA GCA Ser Gly Leu Tyr Ile Phe Arg Asn Glu Arg Glu Glu Glu Lys Glu Ala 2840 2845 2850	8781			
10	GCA AAA TAT GTG GAG GCC CAA CAA AAG AGA CTA GAA GCC TTA TTC ACT Ala Lys Tyr Val Glu Ala Gln Gln Lys Arg Leu Glu Ala Leu Phe Thr 2855 2860 2865	8829			
15	AAA ATT CAG GAG GAA TTT GAA GAA CAT GAA GAA AAC ACA ACA AAA CCA Lys Ile Gln Glu Glu Phe Glu Glu His Glu Glu Asn Thr Thr Lys Pro 2870 2875 2880	8877			
20	TAT TTA CCA TCA CGT GCA CTA ACA AGA CAG CAA GTT CGT GCT TTG CAA Tyr Leu Pro Ser Arg Ala Leu Thr Arg Gln Gln Val Arg Ala Leu Gln 2885 2890 2895	8925			
25	GAT GGT GCA GAG CTT TAT GAA GCA GTG AAG AAT GCA GCA GAC CCA GCT Asp Gly Ala Glu Leu Tyr Glu Ala Val Lys Asn Ala Ala Asp Pro Ala 2900 2905 2910 2915	8973			
30	TAC CTT GAG GGT TAT TTC AGT GAA GAG CAG TTA AGA GCC TTG AAT AAT Tyr Leu Glu Gly Tyr Phe Ser Glu Glu Gln Leu Arg Ala Leu Asn Asn 2920 2925 2930	9021			
35	CAC AGG CAA ATG TTG AAT GAT AAG AAA CAA GCT CAG ATC CAG TTG GAA His Arg Gln Met Leu Asn Asp Lys Lys Gln Ala Gln Ile Gln Leu Glu 2935 2940 2945	9069			
40	ATT AGG AAG GCC ATG GAA TCT GCT GAA CAA AAG GAA CAA GGT TTA TCA Ile Arg Lys Ala Met Glu Ser Ala Glu Gln Lys Glu Gln Gly Leu Ser 2950 2955 2960	9117			
45	AGG GAT GTC ACA ACC GTG TGG AAG TTG CGT ATT GTA AGC TAT TCA AAA Arg Asp Val Thr Thr Val Trp Lys Leu Arg Ile Val Ser Tyr Ser Lys 2965 2970 2975	9165			
50	AAA GAA AAA GAT TCA GTT ATA CTG AGT ATT TGG CGT CCA TCA TCA GAT Lys Glu Lys Asp Ser Val Ile Leu Ser Ile Trp Arg Pro Ser Ser Asp 2980 2985 2990 2995	9213			
55	TTA TAT TCT CTG TTA ACA GAA GGA AAG AGA TAC AGA ATT TAT CAT CTT Leu Tyr Ser Leu Leu Thr Glu Gly Lys Arg Tyr Arg Ile Tyr His Leu 3000 3005 3010	9261			
60	GCA ACT TCA AAA TCT AAA AGT AAA TCT GAA AGA GCT AAC ATA CAG TTA Ala Thr Ser Lys Ser Lys Ser Lys Ser Glu Arg Ala Asn Ile Gln Leu 3015 3020 3025	9309			
	GCA GCG ACA AAA AAA ACT CAG TAT CAA CAA CTA CCG GTT TCA GAT GAA Ala Ala Thr Lys Lys Thr Gln Tyr Gln Gln Leu Pro Val Ser Asp Glu 3030 3035 3040	9357			
	ATT TTA TTT CAG ATT TAC CAG CCA CGG GAG CCC CTT CAC TTC AGC AAA Ile Leu Phe Gln Ile Tyr Gln Pro Arg Glu Pro Leu His Phe Ser Lys 3045 3050 3055	9405			
	TTT TTA GAT CCA GAC TTT CAG CCA TCT TGT TCT GAG GTG GAC CTA ATA Phe Leu Asp Pro Asp Phe Gln Pro Ser Cys Ser Glu Val Asp Leu Ile 3060 3065 3070 3075	9453			

5	GGA TTT GTC GTT TCT GTT GTG AAA AAA ACA GGA CTT GCC CCT TTC GTC Gly Phe Val Val Ser Val Val Lys Lys Thr Gly Leu Ala Pro Phe Val 3080 3085 3090	9501
10	TAT TTG TCA GAC GAA TGT TAC AAT TTA CTG GCA ATA AAG TTT TGG ATA Tyr Leu Ser Asp Glu Cys Tyr Asn Leu Leu Ala Ile Lys Phe Trp Ile 3095 3100 3105	9549
15	GAC CTT AAT GAG GAC ATT ATT AAG CCT CAT ATG TTA ATT GCT GCA AGC Asp Leu Asn Glu Asp Ile Ile Lys Pro His Met Leu Ile Ala Ala Ser 3110 3115 3120	9597
20	AAC CTC CAG TGG CGA CCA GAA TCC AAA TCA GGC CTT CTT ACT TTA TTT Asn Leu Gln Trp Arg Pro Glu Ser Lys Ser Gly Leu Leu Thr Leu Phe 3125 3130 3135	9645
25	GCT GGA GAT TTT TCT GTG TTT TCT GCT AGT CCA AAA GAG GGC CAC TTT Ala Gly Asp Phe Ser Val Phe Ser Ala Ser Pro Lys Glu Gly His Phe 3140 3145 3150 3155	9693
30	CAA GAG ACA TTC AAC AAA ATG AAA AAT ACT GTT GAG AAT ATT GAC ATA Gln Glu Thr Phe Asn Lys Met Lys Asn Thr Val Glu Asn Ile Asp Ile 3160 3165 3170	9741
35	CTT TGC AAT GAA GCA GAA AAC AAG CTT ATG CAT ATA CTG CAT GCA AAT Leu Cys Asn Glu Ala Glu Asn Lys Leu Met His Ile Leu His Ala Asn 3175 3180 3185	9789
40	GAT CCC AAG TGG TCC ACC CCA ACT AAA GAC TGT ACT TCA GGG CCG TAC Asp Pro Lys Trp Ser Thr Pro Thr Lys Asp Cys Thr Ser Gly Pro Tyr 3190 3195 3200	9837
45	ACT GCT CAA ATC ATT CCT GGT ACA GGA AAC AAG CTT CTG ATG TCT TCT Thr Ala Gln Ile Ile Pro Gly Thr Gly Asn Lys Leu Leu Met Ser Ser 3205 3210 3215	9885
50	CCT AAT TGT GAG ATA TAT TAT CAA AGT CCT TTA TCA CTT TGT ATG GCC Pro Asn Cys Glu Ile Tyr Tyr Gln Ser Pro Leu Ser Leu Cys Met Ala 3220 3225 3230 3235	9933
55	AAA AGG AAG TCT GTT TCC ACA CCT GTC TCA GCC CAG ATG ACT TCA AAG Lys Arg Lys Ser Val Ser Thr Pro Val Ser Ala Gln Met Thr Ser Lys 3240 3245 3250	9981
60	TCT TGT AAA GGG GAG AAA GAG ATT GAT GAC CAA AAG AAC TGC AAA AAG Ser Cys Lys Gly Glu Lys Glu Ile Asp Asp Gln Lys Asn Cys Lys Lys 3255 3260 3265	10029
65	AGA AGA GCC TTG GAT TTC TTG AGT AGA CTG CCT TTA CCT CCA CCT GTT Arg Arg Ala Leu Asp Phe Leu Ser Arg Leu Pro Leu Pro Pro Pro Val 3270 3275 3280	10077
70	AGT CCC ATT TGT ACA TTT GTT TCT CCG GCT GCA CAG AAG GCA TTT CAG Ser Pro Ile Cys Thr Phe Val Ser Pro Ala Ala Gln Lys Ala Phe Gln 3285 3290 3295	10125
75	CCA CCA AGG AGT TGT GGC ACC AAA TAC GAA ACA CCC ATA AAG AAA AAA Pro Pro Arg Ser Cys Gly Thr Lys Tyr Glu Thr Pro Ile Lys Lys Lys 3300 3305 3310 3315	10173

GAA CTG AAT TCT CCT CAG ATG ACT CCA TTT AAA AAA TTC AAT GAA ATT 10221  
 Glu Leu Asn Ser Pro Gln Met Thr Pro Phe Lys Lys Phe Asn Glu Ile  
 3320 3325 3330  
 5 TCT CTT TTG GAA AGT AAT TCA ATA GCT GAC GAA GAA CTT GCA TTG ATA 10269  
 Ser Leu Leu Glu Ser Asn Ser Ile Ala Asp Glu Glu Leu Ala Leu Ile  
 3335 3340 3345  
 10 AAT ACC CAA GCT CTT TTG TCT GGT TCA ACA GGA GAA AAA CAA TTT ATA 10317  
 Asn Thr Gln Ala Leu Leu Ser Gly Ser Thr Gly Glu Lys Gln Phe Ile  
 3350 3355 3360  
 15 TCT GTC AGT GAA TCC ACT AGG ACT GCT CCC ACC AGT TCA GAA GAT TAT 10365  
 Ser Val Ser Glu Ser Thr Arg Thr Ala Pro Thr Ser Ser Glu Asp Tyr  
 3365 3370 3375  
 CTC AGA CTG AAA CGA CGT TGT ACT ACA TCT CTG ATC AAA GAA CAG GAG 10413  
 Leu Arg Leu Lys Arg Arg Cys Thr Thr Ser Leu Ile Lys Glu Gln Glu  
 3380 3385 3390 3395  
 20 AGT TCC CAG GCC AGT ACG GAA GAA TGT GAG AAA AAT AAG CAG GAC ACA 10461  
 Ser Ser Gln Ala Ser Thr Glu Glu Cys Glu Lys Asn Lys Gln Asp Thr  
 3400 3405 3410  
 25 ATT ACA ACT AAA AAA TAT ATC TAA 10485  
 Ile Thr Thr Lys Lys Tyr Ile  
 3415

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(2) INFORMATION FOR SEQ ID NO:11:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 3418 amino acids  
 35 (B) TYPE: amino acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein  
 40 (v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

45 Met Pro Ile Gly Ser Lys Glu Arg Pro Thr Phe Phe Glu Ile Phe Lys  
 1 5 10 15  
 Thr Arg Cys Asn Lys Ala Asp Leu Gly Pro Ile Ser Leu Asn Trp Phe  
 20 25 30  
 Glu Glu Leu Ser Ser Glu Ala Pro Pro Tyr Asn Ser Glu Pro Ala Glu  
 35 40 45  
 50 Glu Ser Glu His Lys Asn Asn Asn Tyr Glu Pro Asn Leu Phe Lys Thr  
 50 55 60  
 Pro Gln Arg Lys Pro Ser Tyr Asn Gln Leu Ala Ser Thr Pro Ile Ile  
 65 70 75 80  
 Phe Lys Glu Gln Gly Leu Thr Leu Pro Leu Tyr Gln Ser Pro Val Lys  
 85 90 95  
 55 Glu Leu Asp Lys Phe Lys Leu Asp Leu Gly Arg Asn Val Pro Asn Ser  
 100 105 110  
 Arg His Lys Ser Leu Arg Thr Val Lys Thr Lys Met Asp Gln Ala Asp  
 115 120 125  
 60 Asp Val Ser Cys Pro Leu Leu Asn Ser Cys Leu Ser Glu Ser Pro Val  
 130 135 140  
 Val Leu Gln Cys Thr His Val Thr Pro Gln Arg Asp Lys Ser Val Val

	145		150		155		160
	Cys Gly Ser Leu Phe His Thr Pro Lys Phe Val Lys Gly Arg Gln Thr						
		165		170		175	
5	Pro Lys His Ile Ser Glu Ser Leu Gly Ala Glu Val Asp Pro Asp Met						
	Ser Trp Ser Ser Ser Leu Ala Thr Pro Pro Thr Leu Ser Ser Thr Val	180	185	190			
		195	200	205			
10	Leu Ile Val Arg Asn Glu Glu Ala Ser Glu Thr Val Phe Pro His Asp						
	Thr Thr Ala Asn Val Lys Ser Tyr Phe Ser Asn His Asp Glu Ser Leu	210	215	220			
		225	230	235			240
	Lys Lys Asn Asp Arg Phe Ile Ala Ser Val Thr Asp Ser Glu Asn Thr						
		245	250	255			
15	Asn Gln Arg Glu Ala Ala Ser His Gly Phe Gly Lys Thr Ser Gly Asn						
	Ser Phe Lys Val Asn Ser Cys Lys Asp His Ile Gly Lys Ser Met Pro	260	265	270			
		275	280	285			
20	Asn Val Leu Glu Asp Glu Val Tyr Glu Thr Val Val Asp Thr Ser Glu						
	Glu Asp Ser Phe Ser Leu Cys Phe Ser Lys Cys Arg Thr Lys Asn Leu	290	295	300			
		305	310	315			320
	Gln Lys Val Arg Thr Ser Lys Thr Arg Lys Lys Ile Phe His Glu Ala						
		325	330	335			
25	Asn Ala Asp Glu Cys Glu Lys Ser Lys Asn Gln Val Lys Glu Lys Tyr						
	Ser Phe Val Ser Glu Val Glu Pro Asn Asp Thr Asp Pro Leu Asp Ser	340	345	350			
		355	360	365			
30	Asn Val Ala His Gln Lys Pro Phe Glu Ser Gly Ser Asp Lys Ile Ser						
	Lys Glu Val Val Pro Ser Leu Ala Cys Glu Trp Ser Gln Leu Thr Leu	370	375	380			
		385	390	395			400
	Ser Gly Leu Asn Gly Ala Gln Met Glu Lys Ile Pro Leu Leu His Ile						
		405	410	415			
35	Ser Ser Cys Asp Gln Asn Ile Ser Glu Lys Asp Leu Leu Asp Thr Glu						
	Asn Lys Arg Lys Lys Asp Phe Leu Thr Ser Glu Asn Ser Leu Pro Arg	420	425	430			
		435	440	445			
40	Ile Ser Ser Leu Pro Lys Ser Glu Lys Pro Leu Asn Glu Glu Thr Val						
	Val Asn Lys Arg Asp Glu Glu Gln His Leu Glu Ser His Thr Asp Cys	450	455	460			
		465	470	475			480
	Ile Leu Ala Val Lys Gln Ala Ile Ser Gly Thr Ser Pro Val Ala Ser						
		485	490	495			
45	Ser Phe Gln Gly Ile Lys Lys Ser Ile Phe Arg Ile Arg Glu Ser Pro						
	Lys Glu Thr Phe Asn Ala Ser Phe Ser Gly His Met Thr Asp Pro Asn	500	505	510			
		515	520	525			
50	Phe Lys Lys Glu Thr Glu Ala Ser Glu Ser Gly Leu Glu Ile His Thr						
	Val Cys Ser Gln Lys Glu Asp Ser Leu Cys Pro Asn Leu Ile Asp Asn	530	535	540			
		545	550	555			560
	Gly Ser Trp Pro Ala Thr Thr Thr Gln Asn Ser Val Ala Leu Lys Asn						
		565	570	575			
55	Ala Gly Leu Ile Ser Thr Leu Lys Lys Lys Thr Asn Lys Phe Ile Tyr						
	Ala Ile His Asp Glu Thr Ser Tyr Lys Gly Lys Lys Ile Pro Lys Asp	580	585	590			
		595	600	605			
60	Gln Lys Ser Glu Leu Ile Asn Cys Ser Ala Gln Phe Glu Ala Asn Ala						
	Phe Glu Ala Pro Leu Thr Phe Ala Asn Ala Asp Ser Gly Leu Leu His	610	615	620			
		625	630	635			640

	Ser	Ser	Val	Lys	Arg	Ser	Cys	Ser	Gln	Asn	Asp	Ser	Glu	Glu	Pro	Thr
					645					650					655	
5	Leu	Ser	Leu	Thr	Ser	Ser	Phe	Gly	Thr	Ile	Leu	Arg	Lys	Cys	Ser	Arg
				660					665					670		
	Asn	Glu	Thr	Cys	Ser	Asn	Asn	Thr	Val	Ile	Ser	Gln	Asp	Leu	Asp	Tyr
			675					680					685			
	Lys	Glu	Ala	Lys	Cys	Asn	Lys	Glu	Lys	Leu	Gln	Leu	Phe	Ile	Thr	Pro
		690					695					700				
10	Glu	Ala	Asp	Ser	Leu	Ser	Cys	Leu	Gln	Glu	Gly	Gln	Cys	Glu	Asn	Asp
		705				710					715				720	
	Pro	Lys	Ser	Lys	Lys	Val	Ser	Asp	Ile	Lys	Glu	Glu	Val	Leu	Ala	Ala
					725					730					735	
15	Ala	Cys	His	Pro	Val	Gln	His	Ser	Lys	Val	Glu	Tyr	Ser	Asp	Thr	Asp
				740					745					750		
	Phe	Gln	Ser	Gln	Lys	Ser	Leu	Leu	Tyr	Asp	His	Glu	Asn	Ala	Ser	Thr
			755					760					765			
	Leu	Ile	Leu	Thr	Pro	Thr	Ser	Lys	Asp	Val	Leu	S	Asn	Leu	Val	Met
		770					775						780			
20	Ile	Ser	Arg	Gly	Lys	Glu	Ser	Tyr	Lys	Met	Ser	Asp	Lys	Leu	Lys	Gly
						790					795					800
	Asn	Asn	Tyr	Glu	Ser	Asp	Val	Glu	Leu	Thr	Lys	Asn	Ile	Pro	Met	Glu
					805					810					815	
25	Lys	Asn	Gln	Asp	Val	Cys	Ala	Leu	Asn	Glu	Asn	Tyr	Lys	Asn	Val	Glu
				820					825					830		
	Leu	Leu	Pro	Pro	Glu	Lys	Tyr	Met	Arg	Val	Ala	Ser	Pro	Ser	Arg	Lys
			835					840					845			
	Val	Gln	Phe	Asn	Gln	Asn	Thr	Asn	Leu	Arg	Val	Ile	Gln	Lys	Asn	Gln
		850					855					860				
30	Glu	Glu	Thr	Thr	Ser	Ile	Ser	Lys	Ile	Thr	Val	Asn	Pro	Asp	Ser	Glu
						870					875					880
	Glu	Leu	Phe	Ser	Asp	Asn	Glu	Asn	Asn	Phe	Val	Phe	Gln	Val	Ala	Asn
					885					890					895	
35	Glu	Arg	Asn	Asn	Leu	Ala	Leu	Gly	Asn	Thr	Lys	Glu	Leu	His	Glu	Thr
				900					905					910		
	Asp	Leu	Thr	Cys	Val	Asn	Glu	Pro	Ile	Phe	Lys	Asn	Ser	Thr	Met	Val
			915					920					925			
	Leu	Tyr	Gly	Asp	Thr	Gly	Asp	Lys	Gln	Ala	Thr	Gln	Val	Ser	Ile	Lys
		930					935					940				
40	Lys	Asp	Leu	Val	Tyr	Val	Leu	Ala	Glu	Glu	Asn	Lys	Asn	Ser	Val	Lys
						950					955					960
	Gln	His	Ile	Lys	Met	Thr	Leu	Gly	Gln	Asp	Leu	Lys	Ser	Asp	Ile	Ser
					965					970					975	
45	Leu	Asn	Ile	Asp	Lys	Ile	Pro	Glu	Lys	Asn	Asn	Asp	Tyr	Met	Asn	Lys
				980					985					990		
	Trp	Ala	Gly	Leu	Leu	Gly	Pro	Ile	Ser	Asn	His	Ser	Phe	Gly	Gly	Ser
			995					1000					1005			
	Phe	Arg	Thr	Ala	Ser	Asn	Lys	Glu	Ile	Lys	Leu	Ser	Glu	His	Asn	Ile
			1010				1015					1020				
50	Lys	Lys	Ser	Lys	Met	Phe	Phe	Lys	Asp	Ile	Glu	Glu	Gln	Tyr	Pro	Thr
						1030					1035				104	
	Ser	Leu	Ala	Cys	Val	Glu	Ile	Val	Asn	Thr	Leu	Ala	Leu	Asp	Asn	Gln
					1045					1050					1055	
55	Lys	Lys	Leu	Ser	Lys	Pro	Gln	Ser	Ile	Asn	Thr	Val	Ser	Ala	His	Leu
					1060				1065					1070		
	Gln	Ser	Ser	Val	Val	Val	Ser	Asp	Cys	Lys	Asn	Ser	His	Ile	Thr	Pro
					1075			1080					1085			
	Gln	Met	Leu	Phe	Ser	Lys	Gln	Asp	Phe	Asn	Ser	Asn	His	Asn	Leu	Thr
		1090					1095					1100				
60	Pro	Ser	Gln	Lys	Ala	Glu	Ile	Thr	Glu	Leu	Ser	Thr	Ile	Leu	Glu	Glu
						1110					1115					112
	Ser	Gly	Ser	Gln	Phe	Glu	Phe	Thr	Gln	Phe	Arg	Lys	Pro	Ser	Tyr	Ile

				1125					1130					1135		
	Leu	Gln	Lys	Ser	Thr	Phe	Glu	Val	Pro	Glu	Asn	Gln	Met	Thr	Ile	Leu
				1140					1145					1150		
5	Lys	Thr	Thr	Ser	Glu	Glu	Cys	Arg	Asp	Ala	Asp	Leu	His	Val	Ile	Met
				1155					1160					1165		
	Asn	Ala	Pro	Ser	Ile	Gly	Gln	Val	Asp	Ser	Ser	Lys	Gln	Phe	Glu	Gly
				1170					1175					1180		
	Thr	Val	Glu	Ile	Lys	Arg	Lys	Phe	Ala	Gly	Leu	Leu	Lys	Asn	Asp	Cys
10									1190					1195		120
	Asn	Lys	Ser	Ala	Ser	Gly	Tyr	Leu	Thr	Asp	Glu	Asn	Glu	Val	Gly	Phe
	Arg	Gly	Phe	Tyr	Ser	Ala	His	Gly	Thr	Lys	Leu	Asn	Val	Ser	Thr	Glu
15	Ala	Leu	Gln	Lys	Ala	Val	Lys	Leu	Phe	Ser	Asp	Ile	Glu	Asn	Ile	Ser
	Glu	Glu	Thr	Ser	Ala	Glu	Val	His	Pro	Ile	Ser	Leu	Ser	Ser	Ser	Lys
	Cys	His	Asp	Ser	Val	Val	Ser	Met	Phe	Lys	Ile	Glu	Asn	His	Asn	Asp
20																
	Lys	Thr	Val	Ser	Glu	Lys	Asn	Asn	Lys	Cys	Gln	Leu	Ile	Leu	Gln	Asn
	Asn	Ile	Glu	Met	Thr	Thr	Gly	Thr	Phe	Val	Glu	Glu	Ile	Thr	Glu	Asn
25	Tyr	Lys	Arg	Asn	Thr	Glu	Asn	Glu	Asp	Asn	Lys	Tyr	Thr	Ala	Ala	Ser
	Arg	Asn	Ser	His	Asn	Leu	Glu	Phe	Asp	Gly	Ser	Asp	Ser	Ser	Lys	Asn
	Asp	Thr	Val	Cys	Ile	His	Lys	Asp	Glu	Thr	Asp	Leu	Leu	Phe	Thr	Asp
30																
	Gln	His	Asn	Ile	Cys	Leu	Lys	Leu	Ser	Gly	Gln	Phe	Met	Lys	Glu	Gly
	Asn	Thr	Gln	Ile	Lys	Glu	Asp	Leu	Ser	Asp	Leu	Thr	Phe	Leu	Glu	Val
35	Ala	Lys	Ala	Gln	Glu	Ala	Cys	His	Gly	Asn	Thr	Ser	Asn	Lys	Glu	Gln
	Leu	Thr	Ala	Thr	Lys	Thr	Glu	Gln	Asn	Ile	Lys	Asp	Phe	Glu	Thr	Ser
	Asp	Thr	Phe	Phe	Gln	Thr	Ala	Ser	Gly	Lys	Asn	Ile	Ser	Val	Ala	Lys
40																
	Glu	Ser	Phe	Asn	Lys	Ile	Val	Asn	Phe	Phe	Asp	Gln	Lys	Pro	Glu	Glu
	Leu	His	Asn	Phe	Ser	Leu	Asn	Ser	Glu	Leu	His	Ser	Asp	Ile	Arg	Lys
45	Asn	Lys	Met	Asp	Ile	Leu	Ser	Tyr	Glu	Glu	Thr	Asp	Ile	Val	Lys	His
	Lys	Ile	Leu	Lys	Glu	Ser	Val	Pro	Val	Gly	Thr	Gly	Asn	Gln	Leu	Val
	Thr	Phe	Gln	Gly	Gln	Pro	Glu	Arg	Asp	Glu	Lys	Ile	Lys	Glu	Pro	Thr
50																
	Leu	Leu	Gly	Phe	His	Thr	Ala	Ser	Gly	Lys	Lys	Val	Lys	Ile	Ala	Lys
	Glu	Ser	Leu	Asp	Lys	Val	Lys	Asn	Leu	Phe	Asp	Glu	Lys	Glu	Gln	Gly
55	Thr	Ser	Glu	Ile	Thr	Ser	Phe	Ser	His	Gln	Trp	Ala	Lys	Thr	Leu	Lys
	Tyr	Arg	Glu	Ala	Cys	Lys	Asp	Leu	Glu	Leu	Ala	Cys	Glu	Thr	Ile	Glu
	Ile	Thr	Ala	Ala	Pro	Lys	Cys	Lys	Glu	Met	Gln	Asn	Ser	Leu	Asn	Asn
60																
	Asp	Lys	Asn	Leu	Val	Ser	Ile	Glu	Thr	Val	Val	Pro	Pro	Lys	Leu	Leu

	Ser	Asp	Asn	Leu	Cys	Arg	Gln	Thr	Glu	Asn	Leu	Lys	Thr	Ser	Lys	Ser	
				1620					1625					1630			
5	Ile	Phe	Leu	Lys	Val	Lys	Val	His	Glu	Asn	Val	Glu	Lys	Glu	Thr	Ala	
			1635				1640						1645				
	Lys	Ser	Pro	Ala	Thr	Cys	Tyr	Thr	Asn	Gln	Ser	Pro	Tyr	Ser	Val	Ile	
			1650				1655					1660					
	Glu	Asn	Ser	Ala	Leu	Ala	Phe	Tyr	Thr	Ser	Cys	Ser	Arg	Lys	Thr	Ser	
	1665				1670						1675					168	
10	Val	Ser	Gln	Thr	Ser	Leu	Leu	Glu	Ala	Lys	Lys	Trp	Leu	Arg	Glu	Gly	
				1685						1690					1695		
	Ile	Phe	Asp	Gly	Gln	Pro	Glu	Arg	Ile	Asn	Thr	Ala	Asp	Tyr	Val	Gly	
				1700					1705					1710			
15	Asn	Tyr	Leu	Tyr	Glu	Asn	Asn	Ser	Asn	Ser	Thr	Ile	Ala	Glu	Asn	Asp	
			1715				1720						1725				
	Lys	Asn	His	Leu	Ser	Glu	Lys	Gln	Asp	Thr	Tyr	Leu	Ser	Asn	Ser	Ser	
			1730				1735					1740					
	Met	Ser	Asn	Ser	Tyr	Ser	Tyr	His	Ser	Asp	Glu	Val	Tyr	Asn	Asp	Ser	
	1745				1750						1755					176	
20	Gly	Tyr	Leu	Ser	Lys	Asn	Lys	Leu	Asp	Ser	Gly	Ile	Glu	Pro	Val	Leu	
				1765						1770					1775		
	Lys	Asn	Val	Glu	Asp	Gln	Lys	Asn	Thr	Ser	Phe	Ser	Lys	Val	Ile	Ser	
				1780					1785					1790			
25	Asn	Val	Lys	Asp	Ala	Asn	Ala	Tyr	Pro	Gln	Thr	Val	Asn	Glu	Asp	Ile	
			1795				1800						1805				
	Cys	Val	Glu	Glu	Leu	Val	Thr	Ser	Ser	Ser	Pro	Cys	Lys	Asn	Lys	Asn	
			1810				1815					1820					
	Ala	Ala	Ile	Lys	Leu	Ser	Ile	Ser	Asn	Ser	Asn	Asn	Phe	Glu	Val	Gly	
	1825				1830						1835					184	
30	Pro	Pro	Ala	Phe	Arg	Ile	Ala	Ser	Gly	Lys	Ile	Val	Cys	Val	Ser	His	
				1845						1850					1855		
	Glu	Thr	Ile	Lys	Lys	Val	Lys	Asp	Ile	Phe	Thr	Asp	Ser	Phe	Ser	Lys	
				1860					1865					1870			
35	Val	Ile	Lys	Glu	Asn	Asn	Glu	Asn	Lys	Ser	Lys	Ile	Cys	Gln	Thr	Lys	
			1875				1880						1885				
	Ile	Met	Ala	Gly	Cys	Tyr	Glu	Ala	Leu	Asp	Asp	Ser	Glu	Asp	Ile	Leu	
			1890				1895					1900					
	His	Asn	Ser	Leu	Asp	Asn	Asp	Glu	Cys	Ser	Thr	His	Ser	His	Lys	Val	
	1905				1910						1915					192	
40	Phe	Ala	Asp	Ile	Gln	Ser	Glu	Glu	Ile	Leu	Gln	His	Asn	Gln	Asn	Met	
				1925						1930					1935		
	Ser	Gly	Leu	Glu	Lys	Val	Ser	Lys	Ile	Ser	Pro	Cys	Asp	Val	Ser	Leu	
				1940					1945					1950			
45	Glu	Thr	Ser	Asp	Ile	Cys	Lys	Cys	Ser	Ile	Gly	Lys	Leu	His	Lys	Ser	
			1955				1960						1965				
	Val	Ser	Ser	Ala	Asn	Thr	Cys	Gly	Ile	Phe	Ser	Thr	Ala	Ser	Gly	Lys	
			1970				1975					1980					
	Ser	Val	Gln	Val	Ser	Asp	Ala	Ser	Leu	Gln	Asn	Ala	Arg	Gln	Val	Phe	
	1985				1990						1995					200	
50	Ser	Glu	Ile	Glu	Asp	Ser	Thr	Lys	Gln	Val	Phe	Ser	Lys	Val	Leu	Phe	
				2005						2010					2015		
	Lys	Ser	Asn	Glu	His	Ser	Asp	Gln	Leu	Thr	Arg	Glu	Glu	Asn	Thr	Ala	
				2020					2025					2030			
55	Ile	Arg	Thr	Pro	Glu	His	Leu	Ile	Ser	Gln	Lys	Gly	Phe	Ser	Tyr	Asn	
			2035				2040						2045				
	Val	Val	Asn	Ser	Ser	Ala	Phe	Ser	Gly	Phe	Ser	Thr	Ala	Ser	Gly	Lys	
			2050				2055					2060					
	Gln	Val	Ser	Ile	Leu	Glu	Ser	Ser	Leu	His	Lys	Val	Lys	Gly	Val	Leu	
	2065				2070						2075					208	
60	Glu	Glu	Phe	Asp	Leu	Ile	Arg	Thr	Glu	His	Ser	Leu	His	Tyr	Ser	Pro	
				2085						2090					2095		
	Thr	Ser	Arg	Gln	Asn	Val	Ser	Lys	Ile	Leu	Pro	Arg	Val	Asp	Lys	Arg	

		2100		2105		2110										
	Asn	Pro	Glu	His	Cys	Val	Asn	Ser	Glu	Met	Glu	Lys	Thr	Cys	Ser	Lys
		2115		2120		2125										
5	Glu	Phe	Lys	Leu	Ser	Asn	Asn	Leu	Asn	Val	Glu	Gly	Gly	Ser	Ser	Glu
		2130		2135		2140										
	Asn	Asn	His	Ser	Ile	Lys	Val	Ser	Pro	Tyr	Leu	Ser	Gln	Phe	Gln	Gln
	2145				2150				2155							216
	Asp	Lys	Gln	Gln	Leu	Val	Leu	Gly	Thr	Lys	Val	Ser	Leu	Val	Glu	Asn
10				2165		2170									2175	
	Ile	His	Val	Leu	Gly	Lys	Glu	Gln	Ala	Ser	Pro	Lys	Asn	Val	Lys	Met
		2180				2185								2190		
	Glu	Ile	Gly	Lys	Thr	Glu	Thr	Phe	Ser	Asp	Val	Pro	Val	Lys	Thr	Asn
		2195				2200								2205		
15	Ile	Glu	Val	Cys	Ser	Thr	Tyr	Ser	Lys	Asp	Ser	Glu	Asn	Tyr	Phe	Glu
		2210				2215								2220		
	Thr	Glu	Ala	Val	Glu	Ile	Ala	Lys	Ala	Phe	Met	Glu	Asp	Asp	Glu	Leu
	2225				2230						2235					224
	Thr	Asp	Ser	Lys	Leu	Pro	Ser	His	Ala	Thr	His	Ser	Leu	Phe	Thr	Cys
20				2245		2250										2255
	Pro	Glu	Asn	Glu	Glu	Met	Val	Leu	Ser	Asn	Ser	Arg	Ile	Gly	Lys	Arg
		2260				2265										2270
	Arg	Gly	Glu	Pro	Leu	Ile	Leu	Val	Gly	Glu	Pro	Ser	Ile	Lys	Arg	Asn
		2275				2280								2285		
25	Leu	Leu	Asn	Glu	Phe	Asp	Arg	Ile	Ile	Glu	Asn	Gln	Glu	Lys	Ser	Leu
		2290				2295								2300		
	Lys	Ala	Ser	Lys	Ser	Thr	Pro	Asp	Gly	Thr	Ile	Lys	Asp	Arg	Arg	Leu
	2305					2310					2315					232
	Phe	Met	His	His	Val	Ser	Leu	Glu	Pro	Ile	Thr	Cys	Val	Pro	Phe	Arg
30				2325		2330										2335
	Thr	Thr	Lys	Glu	Arg	Gln	Glu	Ile	Gln	Asn	Pro	Asn	Phe	Thr	Ala	Pro
		2340				2345										2350
	Gly	Gln	Glu	Phe	Leu	Ser	Lys	Ser	His	Leu	Tyr	Glu	His	Leu	Thr	Leu
		2355				2360								2365		
35	Glu	Lys	Ser	Ser	Ser	Asn	Leu	Ala	Val	Ser	Gly	His	Pro	Phe	Tyr	Gln
		2370				2375								2380		
	Val	Ser	Ala	Thr	Arg	Asn	Glu	Lys	Met	Arg	His	Leu	Ile	Thr	Thr	Gly
	2385				2390						2395					240
	Arg	Pro	Thr	Lys	Val	Phe	Val	Pro	Pro	Phe	Lys	Thr	Lys	Ser	His	Phe
40				2405		2410										2415
	His	Arg	Val	Glu	Gln	Cys	Val	Arg	Asn	Ile	Asn	Leu	Glu	Glu	Asn	Arg
		2420				2425										2430
	Gln	Lys	Gln	Asn	Ile	Asp	Gly	His	Gly	Ser	Asp	Asp	Ser	Lys	Asn	Lys
		2435				2440								2445		
45	Ile	Asn	Asp	Asn	Glu	Ile	His	Gln	Phe	Asn	Lys	Asn	Asn	Ser	Asn	Gln
		2450				2455								2460		
	Ala	Ala	Ala	Val	Thr	Phe	Thr	Lys	Cys	Glu	Glu	Glu	Pro	Leu	Asp	Leu
	2465				2470						2475					248
	Ile	Thr	Ser	Leu	Gln	Asn	Ala	Arg	Asp	Ile	Gln	Asp	Met	Arg	Ile	Lys
50				2485		2490										2495
	Lys	Lys	Gln	Arg	Gln	Arg	Val	Phe	Pro	Gln	Pro	Gly	Ser	Leu	Tyr	Leu
		2500				2505										2510
	Ala	Lys	Thr	Ser	Thr	Leu	Pro	Arg	Ile	Ser	Leu	Lys	Ala	Ala	Val	Gly
		2515				2520										2525
55	Gly	Gln	Val	Pro	Ser	Ala	Cys	Ser	His	Lys	Gln	Leu	Tyr	Thr	Tyr	Gly
		2530				2535										2540
	Val	Ser	Lys	His	Cys	Ile	Lys	Ile	Asn	Ser	Lys	Asn	Ala	Glu	Ser	Phe
	2545				2550						2555					256
	Gln	Phe	His	Thr	Glu	Asp	Tyr	Phe	Gly	Lys	Glu	Ser	Leu	Trp	Thr	Gly
60				2565		2570										2575
	Lys	Gly	Ile	Gln	Leu	Ala	Asp	Gly	Gly	Trp	Leu	Ile	Pro	Ser	Asn	Asp
		2580				2585										2590



	Gly	Lys	Ala	Gly	Lys	Glu	Glu	Phe	Tyr	Arg	Ala	Leu	Cys	Asp	Thr	Pro	
			2595					2600					2605				
5	Gly	Val	Asp	Pro	Lys	Leu	Ile	Ser	Arg	Ile	Trp	Val	Tyr	Asn	His	Tyr	
		2610					2615					2620					
	Arg	Trp	Ile	Ile	Trp	Lys	Leu	Ala	Ala	Met	Glu	Cys	Ala	Phe	Pro	Lys	
		2625				2630					2635					264	
	Glu	Phe	Ala	Asn	Arg	Cys	Leu	Ser	Pro	Glu	Arg	Val	Leu	Leu	Gln	Leu	
					2645						2650				2655		
10	Lys	Tyr	Arg	Tyr	Asp	Thr	Glu	Ile	Asp	Arg	Ser	Arg	Arg	Ser	Ala	Ile	
				2660					2665					2670			
	Lys	Lys	Ile	Met	Glu	Arg	Asp	Asp	Thr	Ala	Ala	Lys	Thr	Leu	Val	Leu	
			2675					2680					2685				
15	Cys	Val	Ser	Asp	Ile	Ile	Ser	Leu	Ser	Ala	Asn	Ile	Ser	Glu	Thr	Ser	
		2690					2695					2700					
	Ser	Asn	Lys	Thr	Ser	Ser	Ala	Asp	Thr	Gln	Lys	Val	Ala	Ile	Ile	Glu	
		2705				2710					2715					272	
	Leu	Thr	Asp	Gly	Trp	Tyr	Ala	Val	Lys	Ala	Gln	Leu	Asp	Pro	Pro	Leu	
				2725						2730					2735		
20	Leu	Ala	Val	Leu	Lys	Asn	Gly	Arg	Leu	Thr	Val	Gly	Gln	Lys	Ile	Ile	
				2740					2745					2750			
	Leu	His	Gly	Ala	Glu	Leu	Val	Gly	Ser	Pro	Asp	Ala	Cys	Thr	Pro	Leu	
		2755					2760					2765					
25	Glu	Ala	Pro	Glu	Ser	Leu	Met	Leu	Lys	Ile	Ser	Ala	Asn	Ser	Thr	Arg	
		2770					2775					2780					
	Pro	Ala	Arg	Trp	Tyr	Thr	Lys	Leu	Gly	Phe	Phe	Pro	Asp	Pro	Arg	Pro	
		2785				2790					2795					280	
	Phe	Pro	Leu	Pro	Leu	Ser	Ser	Leu	Phe	Ser	Asp	Gly	Gly	Asn	Val	Gly	
					2805					2810					2815		
30	Cys	Val	Asp	Val	Ile	Ile	Gln	Arg	Ala	Tyr	Pro	Ile	Gln	Trp	Met	Glu	
				2820					2825					2830			
	Lys	Thr	Ser	Ser	Gly	Leu	Tyr	Ile	Phe	Arg	Asn	Glu	Arg	Glu	Glu	Glu	
				2835				2840				2845					
35	Lys	Glu	Ala	Ala	Lys	Tyr	Val	Glu	Ala	Gln	Gln	Lys	Arg	Leu	Glu	Ala	
		2850					2855					2860					
	Leu	Phe	Thr	Lys	Ile	Gln	Glu	Glu	Phe	Glu	Glu	His	Glu	Glu	Asn	Thr	
		2865				2870					2875				288		
	Thr	Lys	Pro	Tyr	Leu	Pro	Ser	Arg	Ala	Leu	Thr	Arg	Gln	Gln	Val	Arg	
				2885						2890					2895		
40	Ala	Leu	Gln	Asp	Gly	Ala	Glu	Leu	Tyr	Glu	Ala	Val	Lys	Asn	Ala	Ala	
				2900					2905					2910			
	Asp	Pro	Ala	Tyr	Leu	Glu	Gly	Tyr	Phe	Ser	Glu	Glu	Gln	Leu	Arg	Ala	
			2915				2920					2925					
45	Leu	Asn	Asn	His	Arg	Gln	Met	Leu	Asn	Asp	Lys	Lys	Gln	Ala	Gln	Ile	
		2930				2935						2940					
	Gln	Leu	Glu	Ile	Arg	Lys	Ala	Met	Glu	Ser	Ala	Glu	Gln	Lys	Glu	Gln	
		2945				2950					2955				296		
	Gly	Leu	Ser	Arg	Asp	Val	Thr	Thr	Val	Trp	Lys	Leu	Arg	Ile	Val	Ser	
				2965						2970					2975		
50	Tyr	Ser	Lys	Lys	Glu	Lys	Asp	Ser	Val	Ile	Leu	Ser	Ile	Trp	Arg	Pro	
				2980					2985					2990			
	Ser	Ser	Asp	Leu	Tyr	Ser	Leu	Leu	Thr	Glu	Gly	Lys	Arg	Tyr	Arg	Ile	
			2995				3000						3005				
55	Tyr	His	Leu	Ala	Thr	Ser	Lys	Ser	Lys	Ser	Lys	Ser	Glu	Arg	Ala	Asn	
		3010					3015					3020					
	Ile	Gln	Leu	Ala	Ala	Thr	Lys	Lys	Thr	Gln	Tyr	Gln	Gln	Leu	Pro	Val	
		3025				3030					3035				304		
	Ser	Asp	Glu	Ile	Leu	Phe	Gln	Ile	Tyr	Gln	Pro	Arg	Glu	Pro	Leu	His	
				3045						3050					3055		
60	Phe	Ser	Lys	Phe	Leu	Asp	Pro	Asp	Phe	Gln	Pro	Ser	Cys	Ser	Glu	Val	
				3060					3065					3070			
	Asp	Leu	Ile	Gly	Phe	Val	Val	Ser	Val	Val	Lys	Lys	Thr	Gly	Leu	Ala	

	3075	3080	3085
	Pro Phe Val Tyr Leu Ser Asp Glu Cys Tyr Asn Leu Leu Ala Ile Lys		
	3090	3095	3100
5	Phe Trp Ile Asp Leu Asn Glu Asp Ile Ile Lys Pro His Met Leu Ile		
	3105	3110	3115
	Ala Ala Ser Asn Leu Gln Trp Arg Pro Glu Ser Lys Ser Gly Leu Leu		
	3125	3130	3135
10	Thr Leu Phe Ala Gly Asp Phe Ser Val Phe Ser Ala Ser Pro Lys Glu		
	3140	3145	3150
	Gly His Phe Gln Glu Thr Phe Asn Lys Met Lys Asn Thr Val Glu Asn		
	3155	3160	3165
	Ile Asp Ile Leu Cys Asn Glu Ala Glu Asn Lys Leu Met His Ile Leu		
	3170	3175	3180
15	His Ala Asn Asp Pro Lys Trp Ser Thr Pro Thr Lys Asp Cys Thr Ser		
	3185	3190	3195
	Gly Pro Tyr Thr Ala Gln Ile Ile Pro Gly Thr Gly Asn Lys Leu Leu		
	3205	3210	3215
20	Met Ser Ser Pro Asn Cys Glu Ile Tyr Tyr Gln Ser Pro Leu Ser Leu		
	3220	3225	3230
	Cys Met Ala Lys Arg Lys Ser Val Ser Thr Pro Val Ser Ala Gln Met		
	3235	3240	3245
	Thr Ser Lys Ser Cys Lys Gly Glu Lys Glu Ile Asp Asp Gln Lys Asn		
	3250	3255	3260
25	Cys Lys Lys Arg Arg Ala Leu Asp Phe Leu Ser Arg Leu Pro Leu Pro		
	3265	3270	3275
	Pro Pro Val Ser Pro Ile Cys Thr Phe Val Ser Pro Ala Ala Gln Lys		
	3285	3290	3295
30	Ala Phe Gln Pro Pro Arg Ser Cys Gly Thr Lys Tyr Glu Thr Pro Ile		
	3300	3305	3310
	Lys Lys Lys Glu Leu Asn Ser Pro Gln Met Thr Pro Phe Lys Lys Phe		
	3315	3320	3325
	Asn Glu Ile Ser Leu Leu Glu Ser Asn Ser Ile Ala Asp Glu Glu Leu		
	3330	3335	3340
35	Ala Leu Ile Asn Thr Gln Ala Leu Leu Ser Gly Ser Thr Gly Glu Lys		
	3345	3350	3355
	Gln Phe Ile Ser Val Ser Glu Ser Thr Arg Thr Ala Pro Thr Ser Ser		
	3365	3370	3375
40	Glu Asp Tyr Leu Arg Leu Lys Arg Arg Cys Thr Thr Ser Leu Ile Lys		
	3380	3385	3390
	Glu Gln Glu Ser Ser Gln Ala Ser Thr Glu Glu Cys Glu Lys Asn Lys		
	3395	3400	3405
	Gln Asp Thr Ile Thr Thr Lys Lys Tyr Ile		
	3410	3415	

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(2) INFORMATION FOR SEQ ID NO:12:

(i) SEQUENCE CHARACTERISTICS:

- 50 (A) LENGTH: 10485 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

55

(ix) FEATURE:

- (A) NAME/KEY: Coding Sequence  
 (B) LOCATION: 229...10482  
 (D) OTHER INFORMATION: BRCA2 (OMI5)

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

	GGTGGCGCGA	GCTTCTGAAA	CTAGGCGGCA	GAGGCGGAGC	CGCTGTGGCA	CTGCTGCGCC	60
	TCTGCTGCGC	CTCGGGTGTG	TTTTGCGGCG	GTGGGTCGCC	GCCGGGAGAA	GCGTGAGGGG	120
	ACAGATTGTG	GACCGGCGCG	GTTTTGTGCA	GCTTACTCCG	GCCAAAAAAG	AACTGCACCT	180
5	CTGGAGCGGA	CTTATTTACC	AAGCATTGGA	GGAATATCGT	AGGTAAAA	ATG CCT ATT	237
						Met Pro Ile	
						1	
10	GGA TCC AAA GAG AGG CCA ACA TTT TTT GAA ATT TTT AAG ACA CGC TGC	285					
	Gly Ser Lys Glu Arg Pro Thr Phe Phe Glu Ile Phe Lys Thr Arg Cys						
	5 10 15						
15	AAC AAA GCA GAT TTA GGA CCA ATA AGT CTT AAT TGG TTT GAA GAA CTT	333					
	Asn Lys Ala Asp Leu Gly Pro Ile Ser Leu Asn Trp Phe Glu Glu Leu						
	20 25 30 35						
20	TCT TCA GAA GCT CCA CCC TAT AAT TCT GAA CCT GCA GAA GAA TCT GAA	381					
	Ser Ser Glu Ala Pro Pro Tyr Asn Ser Glu Pro Ala Glu Glu Ser Glu						
	40 45 50						
25	CAT AAA AAC AAC AAT TAC GAA CCA AAC CTA TTT AAA ACT CCA CAA AGG	429					
	His Lys Asn Asn Asn Tyr Glu Pro Asn Leu Phe Lys Thr Pro Gln Arg						
	55 60 65						
30	AAA CCA TCT TAT AAT CAG CTG GCT TCA ACT CCA ATA ATA TTC AAA GAG	477					
	Lys Pro Ser Tyr Asn Gln Leu Ala Ser Thr Pro Ile Ile Phe Lys Glu						
	70 75 80						
35	CAA GGG CTG ACT CTG CCG CTG TAC CAA TCT CCT GTA AAA GAA TTA GAT	525					
	Gln Gly Leu Thr Leu Pro Leu Tyr Gln Ser Pro Val Lys Glu Leu Asp						
	85 90 95						
40	AAA TTC AAA TTA GAC TTA GGA AGG AAT GTT CCC AAT AGT AGA CAT AAA	573					
	Lys Phe Lys Leu Asp Leu Gly Arg Asn Val Pro Asn Ser Arg His Lys						
	100 105 110 115						
45	AGT CTT CGC ACA GTG AAA ACT AAA ATG GAT CAA GCA GAT GAT GTT TCC	621					
	Ser Leu Arg Thr Val Lys Thr Lys Met Asp Gln Ala Asp Asp Val Ser						
	120 125 130						
50	TGT CCA CTT CTA AAT TCT TGT CTT AGT GAA AGT CCT GTT GTT CTA CAA	669					
	Cys Pro Leu Leu Asn Ser Cys Leu Ser Glu Ser Pro Val Val Leu Gln						
	135 140 145						
55	TGT ACA CAT GTA ACA CCA CAA AGA GAT AAG TCA GTG GTA TGT GGG AGT	717					
	Cys Thr His Val Thr Pro Gln Arg Asp Lys Ser Val Val Cys Gly Ser						
	150 155 160						
60	TTG TTT CAT ACA CCA AAG TTT GTG AAG GGT CGT CAG ACA CCA AAA CAT	765					
	Leu Phe His Thr Pro Lys Phe Val Lys Gly Arg Gln Thr Pro Lys His						
	165 170 175						
65	ATT TCT GAA AGT CTA GGA GCT GAG GTG GAT CCT GAT ATG TCT TGG TCA	813					
	Ile Ser Glu Ser Leu Gly Ala Glu Val Asp Pro Asp Met Ser Trp Ser						
	180 185 190 195						
70	AGT TCT TTA GCT ACA CCA CCC ACC CTT AGT TCT ACT GTG CTC ATA GTC	861					
	Ser Ser Leu Ala Thr Pro Pro Thr Leu Ser Ser Thr Val Leu Ile Val						
	200 205 210						
75	AGA AAT GAA GAA GCA TCT GAA ACT GTA TTT CCT CAT GAT ACT ACT GCT	909					
	Arg Asn Glu Glu Ala Ser Glu Thr Val Phe Pro His Asp Thr Thr Ala						

	215	220	225	
5	AAT GTG AAA AGC TAT TTT TCC AAT CAT GAT GAA AGT CTG AAG AAA AAT Asn Val Lys Ser Tyr Phe Ser Asn His Asp Glu Ser Leu Lys Lys Asn 230 235 240	957		
10	GAT AGA TTT ATC GCT TCT GTG ACA GAC AGT GAA AAC ACA AAT CAA AGA Asp Arg Phe Ile Ala Ser Val Thr Asp Ser Glu Asn Thr Asn Gln Arg 245 250 255	1005		
15	GAA GCT GCA AGT CAT GGA TTT GGA AAA ACA TCA GGG AAT TCA TTT AAA Glu Ala Ala Ser His Gly Phe Gly Lys Thr Ser Gly Asn Ser Phe Lys 260 265 270 275	1053		
20	GTA AAT AGC TGC AAA GAC CAC ATT GGA AAG TCA ATG CCA CAT GTC CTA Val Asn Ser Cys Lys Asp His Ile Gly Lys Ser Met Pro His Val Leu 280 285 290	1101		
25	GAA GAT GAA GTA TAT GAA ACA GTT GTA GAT ACC TCT GAA GAA GAT AGT Glu Asp Glu Val Tyr Glu Thr Val Val Asp Thr Ser Glu Glu Asp Ser 295 300 305	1149		
30	TTT TCA TTA TGT TTT TCT AAA TGT AGA ACA AAA AAT CTA CAA AAA GTA Phe Ser Leu Cys Phe Ser Lys Cys Arg Thr Lys Asn Leu Gln Lys Val 310 315 320	1197		
35	AGA ACT AGC AAG ACT AGG AAA AAA ATT TTC CAT GAA GCA AAC GCT GAT Arg Thr Ser Lys Thr Arg Lys Lys Ile Phe His Glu Ala Asn Ala Asp 325 330 335	1245		
40	GAA TGT GAA AAA TCT AAA AAC CAA GTG AAA GAA AAA TAC TCA TTT GTA Glu Cys Glu Lys Ser Lys Asn Gln Val Lys Glu Lys Tyr Ser Phe Val 340 345 350 355	1293		
45	TCT GAA GTG GAA CCA AAT GAT ACT GAT CCA TTA GAT TCA AAT GTA GCA Ser Glu Val Glu Pro Asn Asp Thr Asp Pro Leu Asp Ser Asn Val Ala 360 365 370	1341		
50	CAT CAG AAG CCC TTT GAG AGT GGA AGT GAC AAA ATC TCC AAG GAA GTT His Gln Lys Pro Phe Glu Ser Gly Ser Asp Lys Ile Ser Lys Glu Val 375 380 385	1389		
55	GTA CCG TCT TTG GCC TGT GAA TGG TCT CAA CTA ACC CTT TCA GGT CTA Val Pro Ser Leu Ala Cys Glu Trp Ser Gln Leu Thr Leu Ser Gly Leu 390 395 400	1437		
60	AAT GGA GCC CAG ATG GAG AAA ATA CCC CTA TTG CAT ATT TCT TCA TGT Asn Gly Ala Gln Met Glu Lys Ile Pro Leu Leu His Ile Ser Ser Cys 405 410 415	1465		
	GAC CAA AAT ATT TCA GAA AAA GAC CTA TTA GAC ACA GAG AAC AAA AGA Asp Gln Asn Ile Ser Glu Lys Asp Leu Leu Asp Thr Glu Asn Lys Arg 420 425 430 435	1533		
	AAG AAA GAT TTT CTT ACT TCA GAG AAT TCT TTG CCA CGT ATT TCT AGC Lys Lys Asp Phe Leu Thr Ser Glu Asn Ser Leu Pro Arg Ile Ser Ser 440 445 450	1581		
	CTA CCA AAA TCG GAG AAG CCA TTA AAT GAG GAA ACA GTG GTA AAT AAG Leu Pro Lys Ser Glu Lys Pro Leu Asn Glu Glu Thr Val Val Asn Lys 455 460 465	1629		

5	AGA GAT GAA GAG CAG CAT CTT GAA TCT CAT ACA GAC TGC ATT CTT GCA Arg Asp Glu Glu Gln His Leu Glu Ser His Thr Asp Cys Ile Leu Ala 470 475 480	1677
10	GTA AAG CAG GCA ATA TCT GGA ACT TCT CCA GTG GCT TCT TCA TTT CAG Val Lys Gln Ala Ile Ser Gly Thr Ser Pro Val Ala Ser Ser Phe Gln 485 490 495	1725
15	GGT ATC AAA AAG TCT ATA TTC AGA ATA AGA GAA TCA CCT AAA GAG ACT Gly Ile Lys Lys Ser Ile Phe Arg Ile Arg Glu Ser Pro Lys Glu Thr 500 505 510 515	1773
20	TTC AAT GCA AGT TTT TCA GGT CAT ATG ACT GAT CCA AAC TTT AAA AAA Phe Asn Ala Ser Phe Ser Gly His Met Thr Asp Pro Asn Phe Lys Lys 520 525 530	1821
25	GAA ACT GAA GCC TCT GAA AGT GGA CTG GAA ATA CAT ACT GTT TGC TCA Glu Thr Glu Ala Ser Glu Ser Gly Leu Glu Ile His Thr Val Cys Ser 535 540 545	1869
30	CAG AAG GAG GAC TCC TTA TGT CCA AAT TTA ATT GAT AAT GGA AGC TGG Gln Lys Glu Asp Ser Leu Cys Pro Asn Leu Ile Asp Asn Gly Ser Trp 550 555 560	1917
35	CCA GCC ACC ACC ACA CAG AAT TCT GTA GCT TTG AAG AAT GCA GGT TTA Pro Ala Thr Thr Thr Gln Asn Ser Val Ala Leu Lys Asn Ala Gly Leu 565 570 575	1965
40	ATA TCC ACT TTG AAA AAG AAA ACA AAT AAG TTT ATT TAT GCT ATA CAT Ile Ser Thr Leu Lys Lys Lys Thr Asn Lys Phe Ile Tyr Ala Ile His 580 585 590 595	2013
45	GAT GAA ACA TCT TAT AAA GGA AAA AAA ATA CCG AAA GAC CAA AAA TCA Asp Glu Thr Ser Tyr Lys Gly Lys Lys Ile Pro Lys Asp Gln Lys Ser 600 605 610	2061
50	GAA CTA ATT AAC TGT TCT GCC CAG TTT GAA GCA AAT GCT TTT GAA GCA Glu Leu Ile Asn Cys Ser Ala Gln Phe Glu Ala Asn Ala Phe Glu Ala 615 620 625	2109
55	CCA CTT ACA TTT GCA AAT GCT GAT TCA GGT TTA TTG CAT TCT TCT GTG Pro Leu Thr Phe Ala Asn Ala Asp Ser Gly Leu Leu His Ser Ser Val 630 635 640	2157
60	AAA AGA AGC TGT TCA CAG AAT GAT TCT GAA GAA CCA ACT TTG TCC TTA Lys Arg Ser Cys Ser Gln Asn Asp Ser Glu Glu Pro Thr Leu Ser Leu 645 650 655	2205
65	ACT AGC TCT TTT GGG ACA ATT CTG AGG AAA TGT TCT AGA AAT GAA ACA Thr Ser Ser Phe Gly Thr Ile Leu Arg Lys Cys Ser Arg Asn Glu Thr 660 665 670 675	2253
70	TGT TCT AAT AAT ACA GTA ATC TCT CAG GAT CTT GAT TAT AAA GAA GCA Cys Ser Asn Asn Thr Val Ile Ser Gln Asp Leu Asp Tyr Lys Glu Ala 680 685 690	2301
75	AAA TGT AAT AAG GAA AAA CTA CAG TTA TTT ATT ACC CCA GAA GCT GAT Lys Cys Asn Lys Glu Lys Leu Gln Leu Phe Ile Thr Pro Glu Ala Asp 695 700 705	2349

	TCT CTG TCA TGC CTG CAG GAA GGA CAG TGT GAA AAT GAT CCA AAA AGC	2397
	Ser Leu Ser Cys Leu Gln Glu Gly Gln Cys Glu Asn Asp Pro Lys Ser	
	710 715 720	
5	AAA AAA GTT TCA GAT ATA AAA GAA GAG GTC TTG GCT GCA GCA TGT CAC	2445
	Lys Lys Val Ser Asp Ile Lys Glu Glu Val Leu Ala Ala Ala Cys His	
	725 730 735	
10	CCA GTA CAA CAC TCA AAA GTG GAA TAC AGT GAT ACT GAC TTT CAA TCC	2493
	Pro Val Gln His Ser Lys Val Glu Tyr Ser Asp Thr Asp Phe Gln Ser	
	740 745 750 755	
15	CAG AAA AGT CTT TTA TAT GAT CAT GAA AAT GCC AGC ACT CTT ATT TTA	2541
	Gln Lys Ser Leu Leu Tyr Asp His Glu Asn Ala Ser Thr Leu Ile Leu	
	760 765 770	
20	ACT CCT ACT TCC AAG GAT GTT CTG TCA AAC CTA GTC ATG ATT TCT AGA	2589
	Thr Pro Thr Ser Lys Asp Val Leu Ser Asn Leu Val Met Ile Ser Arg	
	775 780 785	
	GGC AAA GAA TCA TAC AAA ATG TCA GAC AAG CTC AAA GGT AAC AAT TAT	2637
	Gly Lys Glu Ser Tyr Lys Met Ser Asp Lys Leu Lys Gly Asn Asn Tyr	
	790 795 800	
25	GAA TCT GAT GTT GAA TTA ACC AAA AAT ATT CCC ATG GAA AAG AAT CAA	2685
	Glu Ser Asp Val Glu Leu Thr Lys Asn Ile Pro Met Glu Lys Asn Gln	
	805 810 815	
30	GAT GTA TGT GCT TTA AAT GAA AAT TAT AAA AAC GTT GAG CTG TTG CCA	2733
	Asp Val Cys Ala Leu Asn Glu Asn Tyr Lys Asn Val Glu Leu Leu Pro	
	820 825 830 835	
35	CCT GAA AAA TAC ATG AGA GTA GCA TCA CCT TCA AGA AAG GTA CAA TTC	2781
	Pro Glu Lys Tyr Met Arg Val Ala Ser Pro Ser Arg Lys Val Gln Phe	
	840 845 850	
40	AAC CAA AAC ACA AAT CTA AGA GTA ATC CAA AAA AAT CAA GAA GAA ACT	2829
	Asn Gln Asn Thr Asn Leu Arg Val Ile Gln Lys Asn Gln Glu Glu Thr	
	855 860 865	
	ACT TCA ATT TCA AAA ATA ACT GTC AAT CCA GAC TCT GAA GAA CTT TTC	2877
	Thr Ser Ile Ser Lys Ile Thr Val Asn Pro Asp Ser Glu Glu Leu Phe	
	870 875 880	
45	TCA GAC AAT GAG AAT AAT TTT GTC TTC CAA ATA GCT AAT GAA AGG AAT	2925
	Ser Asp Asn Glu Asn Asn Phe Val Phe Gln Ile Ala Asn Glu Arg Asn	
	885 890 895	
50	AAT CTT GCT TTA GGA AAT ACT AAG GAA CTT CAT GAA ACA GAC TTG ACT	2973
	Asn Leu Ala Leu Gly Asn Thr Lys Glu Leu His Glu Thr Asp Leu Thr	
	900 905 910 915	
55	TGT GTA AAC GAA CCC ATT TTC AAG AAC TCT ACC ATG GTT TTA TAT GGA	3021
	Cys Val Asn Glu Pro Ile Phe Lys Asn Ser Thr Met Val Leu Tyr Gly	
	920 925 930	
	GAC ACA GGT GAT AAA CAA GCA ACC CAA GTG TCA ATT AAA AAA GAT TTG	3069
	Asp Thr Gly Asp Lys Gln Ala Thr Gln Val Ser Ile Lys Lys Asp Leu	
60	935 940 945	
	GTT TAT GTT CTT GCA GAG GAG AAC AAA AAT AGT GTA AAG CAG CAT ATA	3117

	Val	Tyr	Val	Leu	Ala	Glu	Glu	Asn	Lys	Asn	Ser	Val	Lys	Gln	His	Ile	
			950					955					960				
5	AAA	ATG	ACT	CTA	GGT	CAA	GAT	TTA	AAA	TCG	GAC	ATC	TCC	TTG	AAT	ATA	3165
	Lys	Met	Thr	Leu	Gly	Gln	Asp	Leu	Lys	Ser	Asp	Ile	Ser	Leu	Asn	Ile	
			965				970					975					
10	GAT	AAA	ATA	CCA	GAA	AAA	AAT	AAT	GAT	TAC	ATG	GAC	AAA	TGG	GCA	GGA	3213
	Asp	Lys	Ile	Pro	Glu	Lys	Asn	Asn	Asp	Tyr	Met	Asp	Lys	Trp	Ala	Gly	
	980					985					990					995	
15	CTC	TTA	GGT	CCA	ATT	TCA	AAT	CAC	AGT	TTT	GGA	GGT	AGC	TTC	AGA	ACA	3261
	Leu	Leu	Gly	Pro	Ile	Ser	Asn	His	Ser	Phe	Gly	Gly	Ser	Phe	Arg	Thr	
				1000					1005						1010		
20	GCT	TCA	AAT	AAG	GAA	ATC	AAG	CTC	TCT	GAA	CAT	AAC	ATT	AAG	AAG	AGC	3309
	Ala	Ser	Asn	Lys	Glu	Ile	Lys	Leu	Ser	Glu	His	Asn	Ile	Lys	Lys	Ser	
				1015				1020						1025			
25	AAA	ATG	TTC	TTC	AAA	GAT	ATT	GAA	GAA	CAA	TAT	CCT	ACT	AGT	TTA	GCT	3357
	Lys	Met	Phe	Phe	Lys	Asp	Ile	Glu	Glu	Gln	Tyr	Pro	Thr	Ser	Leu	Ala	
			1030				1035					1040					
30	TGT	GTT	GAA	ATT	GTA	AAT	ACC	TTG	GCA	TTA	GAT	AAT	CAA	AAG	AAA	CTG	3405
	Cys	Val	Glu	Ile	Val	Asn	Thr	Leu	Ala	Leu	Asp	Asn	Gln	Lys	Lys	Leu	
			1045			1050					1055						
35	AGC	AAG	CCT	CAG	TCA	ATT	AAT	ACT	GTA	TCT	GCA	CAT	TTA	CAG	AGT	AGT	3453
	Ser	Lys	Pro	Gln	Ser	Ile	Asn	Thr	Val	Ser	Ala	His	Leu	Gln	Ser	Ser	
	1060				1065				1070					1075			
40	GTA	GTT	GTT	TCT	GAT	TGT	AAA	AAT	AGT	CAT	ATA	ACC	CCT	CAG	ATG	TTA	3501
	Val	Val	Val	Ser	Asp	Cys	Lys	Asn	Ser	His	Ile	Thr	Pro	Gln	Met	Leu	
				1080				1085						1090			
45	TTT	TCC	AAG	CAG	GAT	TTT	AAT	TCA	AAC	CAT	AAT	TTA	ACA	CCT	AGC	CAA	3549
	Phe	Ser	Lys	Gln	Asp	Phe	Asn	Ser	Asn	His	Asn	Leu	Thr	Pro	Ser	Gln	
			1095					1100						1105			
50	AAG	GCA	GAA	ATT	ACA	GAA	CTT	TCT	ACT	ATA	TTA	GAA	GAA	TCA	GGA	AGT	3597
	Lys	Ala	Glu	Ile	Thr	Glu	Leu	Ser	Thr	Ile	Leu	Glu	Glu	Ser	Gly	Ser	
			1110				1115					1120					
55	CAG	TTT	GAA	TTT	ACT	CAG	TTT	AGA	AAA	CCA	AGC	TAC	ATA	TTG	CAG	AAG	3645
	Gln	Phe	Glu	Phe	Thr	Gln	Phe	Arg	Lys	Pro	Ser	Tyr	Ile	Leu	Gln	Lys	
			1125			1130					1135						
60	AGT	ACA	TTT	GAA	GTG	CCT	GAA	AAC	CAG	ATG	ACT	ATC	TTA	AAG	ACC	ACT	3693
	Ser	Thr	Phe	Glu	Val	Pro	Glu	Asn	Gln	Met	Thr	Ile	Leu	Lys	Thr	Thr	
	1140					1145				1150				1155			
65	TCT	GAG	GAA	TGC	AGA	GAT	GCT	GAT	CTT	CAT	GTC	ATA	ATG	AAT	GCC	CCA	3741
	Ser	Glu	Glu	Cys	Arg	Asp	Ala	Asp	Leu	His	Val	Ile	Met	Asn	Ala	Pro	
				1160				1165						1170			
70	TCG	ATT	GGT	CAG	GTA	GAC	AGC	AGC	AAG	CAA	TTT	GAA	GGT	ACA	GTT	GAA	3789
	Ser	Ile	Gly	Gln	Val	Asp	Ser	Ser	Lys	Gln	Phe	Glu	Gly	Thr	Val	Glu	
				1175				1180					1185				
75	ATT	AAA	CGG	AAG	TTT	GCT	GGC	CTG	TTG	AAA	AAT	GAC	TGT	AAC	AAA	AGT	3837
	Ile	Lys	Arg	Lys	Phe	Ala	Gly	Leu	Leu	Lys	Asn	Asp	Cys	Asn	Lys	Ser	

	1190	1195	1200	
5	GCT TCT GGT TAT TTA ACA GAT GAA AAT GAA GTG GGG TTT AGG GGC TTT Ala Ser Gly Tyr Leu Thr Asp Glu Asn Glu Val Gly Phe Arg Gly Phe 1205 1210 1215	3885		
10	TAT TCT GCT CAT GGC ACA AAA CTG AAT GTT TCT ACT GAA GCT CTG CAA Tyr Ser Ala His Gly Thr Lys Leu Asn Val Ser Thr Glu Ala Leu Gln 1220 1225 1230 1235	3933		
15	AAA GCT GTG AAA CTG TTT AGT GAT ATT GAG AAT ATT AGT GAG GAA ACT Lys Ala Val Lys Leu Phe Ser Asp Ile Glu Asn Ile Ser Glu Glu Thr 1240 1245 1250	3981		
20	TCT GCA GAG GTA CAT CCA ATA AGT TTA TCT TCA AGT AAA TGT CAT GAT Ser Ala Glu Val His Pro Ile Ser Leu Ser Ser Ser Lys Cys His Asp 1255 1260 1265	4029		
25	TCT GTT GTT TCA ATG TTT AAG ATA GAA AAT CAT AAT GAT AAA ACT GTA Ser Val Val Ser Met Phe Lys Ile Glu Asn His Asn Asp Lys Thr Val 1270 1275 1280	4077		
30	AGT GAA AAA AAT AAT AAA TGC CAA CTG ATA TTA CAA AAT AAT ATT GAA Ser Glu Lys Asn Asn Lys Cys Gln Leu Ile Leu Gln Asn Asn Ile Glu 1285 1290 1295	4125		
35	ATG ACT ACT GGC ACT TTT GTT GAA GAA ATT ACT GAA AAT TAC AAG AGA Met Thr Thr Gly Thr Phe Val Glu Glu Ile Thr Glu Asn Tyr Lys Arg 1300 1305 1310 1315	4173		
40	AAT ACT GAA AAT GAA GAT AAC AAA TAT ACT GCT GCC AGT AGA AAT TCT Asn Thr Glu Asn Glu Asp Asn Lys Tyr Thr Ala Ala Ser Arg Asn Ser 1320 1325 1330	4221		
45	CAT AAC TTA GAA TTT GAT GGC AGT GAT TCA AGT AAA AAT GAT ACT GTT His Asn Leu Glu Phe Asp Gly Ser Asp Ser Ser Lys Asn Asp Thr Val 1335 1340 1345	4269		
50	TGT ATT CAT AAA GAT GAA ACG GAC TTG CTA TTT ACT GAT CAG CAC AAC Cys Ile His Lys Asp Glu Thr Asp Leu Leu Phe Thr Asp Gln His Asn 1350 1355 1360	4317		
55	ATA TGT CTT AAA TTA TCT GGC CAG TTT ATG AAG GAG GGA AAC ACT CAG Ile Cys Leu Lys Leu Ser Gly Gln Phe Met Lys Glu Gly Asn Thr Gln 1365 1370 1375	4365		
60	ATT AAA GAA GAT TTG TCA GAT TTA ACT TTT TTG GAA GTT GCG AAA GCT Ile Lys Glu Asp Leu Ser Asp Leu Thr Phe Leu Glu Val Ala Lys Ala 1380 1385 1390 1395	4413		
65	CAA GAA GCA TGT CAT GGT AAT ACT TCA AAT AAA GAA CAG TTA ACT GCT Gln Glu Ala Cys His Gly Asn Thr Ser Asn Lys Glu Gln Leu Thr Ala 1400 1405 1410	4461		
70	ACT AAA ACG GAG CAA AAT ATA AAA GAT TTT GAG ACT TCT GAT ACA TTT Thr Lys Thr Glu Gln Asn Ile Lys Asp Phe Glu Thr Ser Asp Thr Phe 1415 1420 1425	4509		
75	TTT CAG ACT GCA AGT GGG AAA AAT ATT AGT GTC GCC AAA GAG TCA TTT Phe Gln Thr Ala Ser Gly Lys Asn Ile Ser Val Ala Lys Glu Ser Phe 1430 1435 1440	4557		



5	AAT AAA ATT GTA AAT TTC TTT GAT CAG AAA CCA GAA GAA TTG CAT AAC Asn Lys Ile Val Asn Phe Phe Asp Gln Lys Pro Glu Glu Leu His Asn 1445 1450 1455	4605
10	TTT TCC TTA AAT TCT GAA TTA CAT TCT GAC ATA AGA AAG AAC AAA ATG Phe Ser Leu Asn Ser Glu Leu His Ser Asp Ile Arg Lys Asn Lys Met 1460 1465 1470 1475	4653
15	GAC ATT CTA AGT TAT GAG GAA ACA GAC ATA GTT AAA CAC AAA ATA CTG Asp Ile Leu Ser Tyr Glu Glu Thr Asp Ile Val Lys His Lys Ile Leu 1480 1485 1490	4701
20	AAA GAA AGT GTC CCA GTT GGT ACT GGA AAT CAA CTA GTG ACC TTC CAG Lys Glu Ser Val Pro Val Gly Thr Gly Asn Gln Leu Val Thr Phe Gln 1495 1500 1505	4749
25	GGA CAA CCC GAA CGT GAT GAA AAG ATC AAA GAA CCT ACT CTG TTG GGT Gly Gln Pro Glu Arg Asp Glu Lys Ile Lys Glu Pro Thr Leu Leu Gly 1510 1515 1520	4797
30	TTT CAT ACA GCT AGC GGG AAA AAA GTT AAA ATT GCA AAG GAA TCT TTG Phe His Thr Ala Ser Gly Lys Lys Val Lys Ile Ala Lys Glu Ser Leu 1525 1530 1535	4845
35	GAC AAA GTG AAA AAC CTT TTT GAT GAA AAA GAG CAA GGT ACT AGT GAA Asp Lys Val Lys Asn Leu Phe Asp Glu Lys Glu Gln Gly Thr Ser Glu 1540 1545 1550 1555	4893
40	ATC ACC AGT TTT AGC CAT CAA TGG GCA AAG ACC CTA AAG TAC AGA GAG Ile Thr Ser Phe Ser His Gln Trp Ala Lys Thr Leu Lys Tyr Arg Glu 1560 1565 1570	4941
45	GCC TGT AAA GAC CTT GAA TTA GCA TGT GAG ACC ATT GAG ATC ACA GCT Ala Cys Lys Asp Leu Glu Leu Ala Cys Glu Thr Ile Glu Ile Thr Ala 1575 1580 1585	4989
50	GCC CCA AAG TGT AAA GAA ATG CAG AAT TCT CTC AAT AAT GAT AAA AAC Ala Pro Lys Cys Lys Glu Met Gln Asn Ser Leu Asn Asn Asp Lys Asn 1590 1595 1600	5037
55	CTT GTT TCT ATT GAG ACT GTG GTG CCA CCT AAG CTC TTA AGT GAT AAT Leu Val Ser Ile Glu Thr Val Val Pro Pro Lys Leu Leu Ser Asp Asn 1605 1610 1615	5085
60	TTA TGT AGA CAA ACT GAA AAT CTC AAA ACA TCA AAA AGT ATC TTT TTG Leu Cys Arg Gln Thr Glu Leu Leu Lys Thr Ser Lys Ser Ile Phe Leu 1620 1625 1630 1635	5133
65	AAA GTT AAA GTA CAT GAA AAT GTA GAA AAA GAA ACA GCA AAA AGT CCT Lys Val Lys Val His Glu Asn Val Glu Lys Glu Thr Ala Lys Ser Pro 1640 1645 1650	5181
70	GCA ACT TGT TAC ACA AAT CAG TCC CCT TAT TCA GTC ATT GAA AAT TCA Ala Thr Cys Tyr Thr Asn Gln Ser Pro Tyr Ser Val Ile Glu Asn Ser 1655 1660 1665	5229
75	GCC TTA GCT TTT TAC ACA AGT TGT AGT AGA AAA ACT TCT GTG AGT CAG Ala Leu Ala Phe Tyr Thr Ser Cys Ser Arg Lys Thr Ser Val Ser Gln 1670 1675 1680	5277

	ACT TCA TTA CTT GAA GCA AAA AAA TGG CTT AGA GAA GGA ATA TTT GAT Thr Ser Leu Leu Glu Ala Lys Lys Trp Leu Arg Glu Gly Ile Phe Asp 1685 1690 1695	5325
5	GGT CAA CCA GAA AGA ATA AAT ACT GCA GAT TAT GTA GGA AAT TAT TTG Gly Gln Pro Glu Arg Ile Asn Thr Ala Asp Tyr Val Gly Asn Tyr Leu 1700 1705 1710 1715	5373
10	TAT GAA AAT AAT TCA AAC AGT ACT ATA GCT GAA AAT GAC AAA AAT CAT Tyr Glu Asn Asn Ser Asn Ser Thr Ile Ala Glu Asn Asp Lys Asn His 1720 1725 1730	5421
15	CTC TCC GAA AAA CAA GAT ACT TAT TTA AGT AAC AGT AGC ATG TCT AAC Leu Ser Glu Lys Gln Asp Thr Tyr Leu Ser Asn Ser Ser Met Ser Asn 1735 1740 1745	5469
20	AGC TAT TCC TAC CAT TCT GAT GAG GTA TAT AAT GAT TCA GGA TAT CTC Ser Tyr Ser Tyr His Ser Asp Glu Val Tyr Asn Asp Ser Gly Tyr Leu 1750 1755 1760	5517
25	TCA AAA AAT AAA CTT GAT TCT GGT ATT GAG CCA GTA TTG AAG AAT GTT Ser Lys Asn Lys Leu Asp Ser Gly Ile Glu Pro Val Leu Lys Asn Val 1765 1770 1775	5565
30	GAA GAT CAA AAA AAC ACT AGT TTT TCC AAA GTA ATA TCC AAT GTA AAA Glu Asp Gln Lys Asn Thr Ser Phe Ser Lys Val Ile Ser Asn Val Lys 1780 1785 1790 1795	5613
35	GAT GCA AAT GCA TAC CCA CAA ACT GTA AAT GAA GAT ATT TGC GTT GAG Asp Ala Asn Ala Tyr Pro Gln Thr Val Asn Glu Asp Ile Cys Val Glu 1800 1805 1810	5661
40	GAA CTT GTG ACT AGC TCT TCA CCC TGC AAA AAT AAA AAT GCA GCC ATT Glu Leu Val Thr Ser Ser Ser Pro Cys Lys Asn Lys Asn Ala Ala Ile 1815 1820 1825	5709
45	AAA TTG TCC ATA TCT AAT AGT AAT AAT TTT GAG GTA GGG CCA CCT GCA Lys Leu Ser Ile Ser Asn Ser Asn Asn Phe Glu Val Gly Pro Pro Ala 1830 1835 1840	5757
50	TTT AGG ATA GCC AGT GGT AAA ATC GTT TGT GTT TCA CAT GAA ACA ATT Phe Arg Ile Ala Ser Gly Lys Ile Val Cys Val Ser His Glu Thr Ile 1845 1850 1855	5805
55	AAA AAA GTG AAA GAC ATA TTT ACA GAC AGT TTC AGT AAA GTA ATT AAG Lys Lys Val Lys Asp Ile Phe Thr Asp Ser Phe Ser Ser Lys Val Ile Lys 1860 1865 1870 1875	5853
60	GAA AAC AAC GAG AAT AAA TCA AAA ATT TGC CAA ACG AAA ATT ATG GCA Glu Asn Asn Glu Asn Lys Ser Lys Ile Cys Gln Thr Lys Ile Met Ala 1880 1885 1890	5901
	GGT TGT TAC GAG GCA TTG GAT GAT TCA GAG GAT ATT CTT CAT AAC TCT Gly Cys Tyr Glu Ala Leu Asp Asp Ser Glu Asp Ile Leu His Asn Ser 1895 1900 1905	5949
	CTA GAT AAT GAT GAA TGT AGC ACG CAT TCA CAT AAG GTT TTT GCT GAC Leu Asp Asn Asp Glu Cys Ser Thr His Ser His Lys Val Phe Ala Asp 1910 1915 1920	5997
	ATT CAG AGT GAA GAA ATT TTA CAA CAT AAC CAA AAT ATG TCT GGA TTG	6045

	Ile Gln Ser Glu Glu Ile Leu Gln His Asn Gln Asn Met Ser Gly Leu	
	1925 1930 1935	
5	GAG AAA GTT TCT AAA ATA TCA CCT TGT GAT GTT AGT TTG GAA ACT TCA Glu Lys Val Ser Lys Ile Ser Pro Cys Asp Val Ser Leu Glu Thr Ser	6093
	1940 1945 1950 1955	
10	GAT ATA TGT AAA TGT AGT ATA GGG AAG CTT CAT AAG TCA GTC TCA TCT Asp Ile Cys Lys Cys Ser Ile Gly Lys Leu His Lys Ser Val Ser Ser	6141
	1960 1965 1970	
15	GCA AAT ACT TGT GGG ATT TTT AGC ACA GCA AGT GGA AAA TCT GTC CAG Ala Asn Thr Cys Gly Ile Phe Ser Thr Ala Ser Gly Lys Ser Val Gln	6189
	1975 1980 1985	
20	GTA TCA GAT GCT TCA TTA CAA AAC GCA AGA CAA GTG TTT TCT GAA ATA Val Ser Asp Ala Ser Leu Gln Asn Ala Arg Gln Val Phe Ser Glu Ile	6237
	1990 1995 2000	
25	GAA GAT AGT ACC AAG CAA GTC TTT TCC AAA GTA TTG TTT AAA AGT AAC Glu Asp Ser Thr Lys Gln Val Phe Ser Lys Val Leu Phe Lys Ser Asn	6285
	2005 2010 2015	
30	GAA CAT TCA GAC CAG CTC ACA AGA GAA GAA AAT ACT GCT ATA CGT ACT Glu His Ser Asp Gln Leu Thr Arg Glu Glu Asn Thr Ala Ile Arg Thr	6333
	2020 2025 2030 2035	
35	CCA GAA CAT TTA ATA TCC CAA AAA GGC TTT TCA TAT AAT GTG GTA AAT Pro Glu His Leu Ile Ser Gln Lys Gly Phe Ser Tyr Asn Val Val Asn	6381
	2040 2045 2050	
40	TCA TCT GCT TTC TCT GGA TTT AGT ACA GCA AGT GGA AAG CAA GTT TCC Ser Ser Ala Phe Ser Gly Phe Ser Thr Ala Ser Gly Lys Gln Val Ser	6429
	2055 2060 2065	
45	ATT TTA GAA AGT TCC TTA CAC AAA GTT AAG GGA GTG TTA GAG GAA TTT Ile Leu Glu Ser Ser Leu His Lys Val Lys Gly Val Leu Glu Glu Phe	6477
	2070 2075 2080	
50	GAT TTA ATC AGA ACT GAG CAT AGT CTT CAC TAT TCA CCT ACG TCT AGA Asp Leu Ile Arg Thr Glu His Ser Leu His Tyr Ser Pro Thr Ser Arg	6525
	2085 2090 2095	
55	CAA AAT GTA TCA AAA ATA CTT CCT CGT GTT GAT AAG AGA AAC CCA GAG Gln Asn Val Ser Lys Ile Leu Pro Arg Val Asp Lys Arg Asn Pro Glu	6573
	2100 2105 2110 2115	
60	CAC TGT GTA AAC TCA GAA ATG GAA AAA ACC TGC AGT AAA GAA TTT AAA His Cys Val Asn Ser Glu Met Glu Lys Thr Cys Ser Lys Glu Phe Lys	6621
	2120 2125 2130	
65	TTA TCA AAT AAC TTA AAT GTT GAA GGT GGT TCT TCA GAA AAT AAT CAC Leu Ser Asn Asn Leu Asn Val Glu Gly Gly Ser Ser Glu Asn Asn His	6669
	2135 2140 2145	
70	TCT ATT AAA GTT TCT CCA TAT CTC TCT CAA TTT CAA CAA GAC AAA CAA Ser Ile Lys Val Ser Pro Tyr Leu Ser Gln Phe Gln Gln Asp Lys Gln	6717
	2150 2155 2160	
75	CAG TTG GTA TTA GGA ACC AAA GTC TCA CTT GTT GAG AAC ATT CAT GTT Gln Leu Val Leu Gly Thr Lys Val Ser Leu Val Glu Asn Ile His Val	6765

	2165	2170	2175	
5	TTG GGA AAA GAA CAG GCT TCA CCT AAA AAC GTA AAA ATG GAA ATT GGT Leu Gly Lys Glu Gln Ala Ser Pro Lys Asn Val Lys Met Glu Ile Gly			6813
	2180	2185	2190	2195
10	AAA ACT GAA ACT TTT TCT GAT GTT CCT GTG AAA ACA AAT ATA GAA GTT Lys Thr Glu Thr Phe Ser Asp Val Pro Val Lys Thr Asn Ile Glu Val			6861
	2200	2205	2210	
15	TGT TCT ACT TAC TCC AAA GAT TCA GAA AAC TAC TTT GAA ACA GAA GCA Cys Ser Thr Tyr Ser Lys Asp Ser Glu Asn Tyr Phe Glu Thr Glu Ala			6909
	2215	2220	2225	
20	GTA GAA ATT GCT AAA GCT TTT ATG GAA GAT GAT GAA CTG ACA GAT TCT Val Glu Ile Ala Lys Ala Phe Met Glu Asp Asp Glu Leu Thr Asp Ser			6957
	2230	2235	2240	
25	AAA CTG CCA AGT CAT GCC ACA CAT TCT CTT TTT ACA TGT CCC GAA AAT Lys Leu Pro Ser His Ala Thr His Ser Leu Phe Thr Cys Pro Glu Asn			7005
	2245	2250	2255	
30	GAG GAA ATG GTT TTG TCA AAT TCA AGA ATT GGA AAA AGA AGA GGA GAG Glu Glu Met Val Leu Ser Asn Ser Arg Ile Gly Lys Arg Arg Gly Glu			7053
	2260	2265	2270	2275
35	CCC CTT ATC TTA GTG GGA GAA CCC TCA ATC AAA AGA AAC TTA TTA AAT Pro Leu Ile Leu Val Gly Glu Pro Ser Ile Lys Arg Asn Leu Leu Asn			7101
	2280	2285	2290	
40	GAA TTT GAC AGG ATA ATA GAA AAT CAA GAA AAA TCC TTA AAG GCT TCA Glu Phe Asp Arg Ile Ile Glu Asn Gln Glu Lys Ser Leu Lys Ala Ser			7149
	2295	2300	2305	
45	AAA AGC ACT CCA GAT GGC ACA ATA AAA GAT CGA AGA TTG TTT ATG CAT Lys Ser Thr Pro Asp Gly Thr Ile Lys Asp Arg Arg Leu Phe Met His			7197
	2310	2315	2320	
50	CAT GTT TCT TTA GAG CCG ATT ACC TGT GTA CCC TTT CGC ACA ACT AAG His Val Ser Leu Glu Pro Ile Thr Cys Val Pro Phe Arg Thr Thr Lys			7245
	2325	2330	2335	
55	GAA CGT CAA GAG ATA CAG AAT CCA AAT TTT ACC GCA CCT GGT CAA GAA Glu Arg Gln Glu Ile Gln Asn Pro Asn Phe Thr Ala Pro Gly Gln Glu			7293
	2340	2345	2350	2355
60	TTT CTG TCT AAA TCT CAT TTG TAT GAA CAT CTG ACT TTG GAA AAA TCT Phe Leu Ser Lys Ser His Leu Tyr Glu His Leu Thr Leu Glu Lys Ser			7341
	2360	2365	2370	
65	TCA AGC AAT TTA GCA GTT TCA GGA CAT CCA TTT TAT CAA GTT TCT GCT Ser Ser Asn Leu Ala Val Ser Gly His Pro Phe Tyr Gln Val Ser Ala			7389
	2375	2380	2385	
70	ACA AGA AAT GAA AAA ATG AGA CAC TTG ATT ACT ACA GGC AGA CCA ACC Thr Arg Asn Glu Lys Met Arg His Leu Ile Thr Thr Gly Arg Pro Thr			7437
	2390	2395	2400	
75	AAA GTC TTT GTT CCA CCT TTT AAA ACT AAA TCA CAT TTT CAC AGA GTT Lys Val Phe Val Pro Pro Phe Lys Thr Lys Ser His Phe His Arg Val			7485
	2405	2410	2415	

5	2420	GAA CAG TGT GTT AGG AAT ATT AAC TTG GAG GAA AAC AGA CAA AAG CAA	7533
		Glu Gln Cys Val Arg Asn Ile Asn Leu Glu Glu Asn Arg Gln Lys Gln	
		2425 2430 2435	
10	2440	AAC ATT GAT GGA CAT GGC TCT GAT GAT AGT AAA AAT AAG ATT AAT GAC	7581
		Asn Ile Asp Gly His Gly Ser Asp Asp Ser Lys Asn Lys Ile Asn Asp	
		2440 2445 2450	
15	2455	AAT GAG ATT CAT CAG TTT AAC AAA AAC AAC TCC AAT CAA GCA GCA GCT	7629
		Asn Glu Ile His Gln Phe Asn Lys Asn Asn Ser Asn Gln Ala Ala Ala	
		2455 2460 2465	
20	2470	GTA ACT TTC ACA AAG TGT GAA GAA GAA CCT TTA GAT TTA ATT ACA AGT	7677
		Val Thr Phe Thr Lys Cys Glu Glu Glu Pro Leu Asp Leu Ile Thr Ser	
		2470 2475 2480	
25	2485	CTT CAG AAT GCC AGA GAT ATA CAG GAT ATG CCA ATT AAG AAG AAA CAA	7725
		Leu Gln Asn Ala Arg Asp Ile Gln Asp Met Arg Ile Lys Lys Lys Gln	
		2485 2490 2495	
30	2500	AGG CAA CGC GTC TTT CCA CAG CCA GGC AGT CTG TAT CTT GCA AAA ACA	7773
		Arg Gln Arg Val Phe Pro Gln Pro Gly Ser Leu Tyr Leu Ala Lys Thr	
		2500 2505 2510 2515	
35	2520	TCC ACT CTG CCT CGA ATC TCT CTG AAA GCA GCA GTA GGA GGC CAA GTT	7821
		Ser Thr Leu Pro Arg Ile Ser Leu Lys Ala Ala Val Gly Gly Gln Val	
		2520 2525 2530	
40	2535	CCC TCT GCG TGT TCT CAT AAA CAG CTG TAT ACG TAT GGC GTT TCT AAA	7869
		Pro Ser Ala Cys Ser His Lys Gln Leu Tyr Thr Tyr Gly Val Ser Lys	
		2535 2540 2545	
45	2550	CAT TGC ATA AAA ATT AAC AGC AAA AAT GCA GAG TCT TTT CAG TTT CAC	7917
		His Cys Ile Lys Ile Asn Ser Lys Asn Ala Glu Ser Phe Gln Phe His	
		2550 2555 2560	
50	2565	ACT GAA GAT TAT TTT GGT AAG GAA AGT TTA TGG ACT GGA AAA GGA ATA	7965
		Thr Glu Asp Tyr Phe Gly Lys Glu Ser Leu Trp Thr Gly Lys Gly Ile	
		2565 2570 2575	
55	2580	CAG TTG GCT GAT GGT GGA TGG CTC ATA CCC TCC AAT GAT GGA AAG GCT	8013
		Gln Leu Ala Asp Gly Gly Trp Leu Ile Pro Ser Asn Asp Gly Lys Ala	
		2580 2585 2590 2595	
60	2600	GGA AAA GAA GAA TTT TAT AGG GCT CTG TGT GAC ACT CCA GGT GTG GAT	8061
		Gly Lys Glu Glu Phe Tyr Arg Ala Leu Cys Asp Thr Pro Gly Val Asp	
		2600 2605 2610	
65	2615	CCA AAG CTT ATT TCT AGA ATT TGG GTT TAT AAT CAC TAT AGA TGG ATC	8109
		Pro Lys Leu Ile Ser Arg Ile Trp Val Tyr Asn His Tyr Arg Trp Ile	
		2615 2620 2625	
70	2630	ATA TGG AAA CTG GCA GCT ATG GAA TGT GCC TTT CCT AAG GAA TTT GCT	8157
		Ile Trp Lys Leu Ala Ala Met Glu Cys Ala Phe Pro Lys Glu Phe Ala	
		2630 2635 2640	
75	2645	AAT AGA TGC CTA AGC CCA GAA AGG GTG CTT CTT CAA CTA AAA TAC AGA	8205
		Asn Arg Cys Leu Ser Pro Glu Arg Val Leu Leu Gln Leu Lys Tyr Arg	
		2645 2650 2655	

	TAT GAT ACG GAA ATT GAT AGA AGC AGA AGA TCG GCT ATA AAA AAG ATA Tyr Asp Thr Glu Ile Asp Arg Ser Arg Arg Ser Ala Ile Lys Lys Ile 2660 2665 2670 2675	8253
5	ATG GAA AGG GAT GAC ACA GCT GCA AAA ACA CTT GTT CTC TGT GTT TCT Met Glu Arg Asp Asp Thr Ala Ala Lys Thr Leu Val Leu Cys Val Ser 2680 2685 2690	8301
10	GAC ATA ATT TCA TTG AGC GCA AAT ATA TCT GAA ACT TCT AGC AAT AAA Asp Ile Ile Ser Leu Ser Ala Asn Ile Ser Glu Thr Ser Ser Asn Lys 2695 2700 2705	8349
15	ACT AGT AGT GCA GAT ACC CAA AAA GTG GCC ATT ATT GAA CTT ACA GAT Thr Ser Ser Ala Asp Thr Gln Lys Val Ala Ile Ile Glu Leu Thr Asp 2710 2715 2720	8397
20	GGG TGG TAT GCT GTT AAG GCC CAG TTA GAT CCT CCC CTC TTA GCT GTC Gly Trp Tyr Ala Val Lys Ala Gln Leu Asp Pro ro Leu Leu Ala Val 2725 2730 2735	8445
25	TTA AAG AAT GGC AGA CTG ACA GTT GGT CAG AAG ATT ATT CTT CAT GGA Leu Lys Asn Gly Arg Leu Thr Val Gly Gln Lys Ile Ile Leu His Gly 2740 2745 2750 2755	8493
	GCA GAA CTG GTG GGC TCT CCT GAT GCC TGT ACA CCT CTT GAA GCC CCA Ala Glu Leu Val Gly Ser Pro Asp Ala Cys Thr Pro Leu Glu Ala Pro 2760 2765 2770	8541
30	GAA TCT CTT ATG TTA AAG ATT TCT GCT AAC AGT ACT CGG CCT GCT CGC Glu Ser Leu Met Leu Lys Ile Ser Ala Asn Ser Thr Arg Pro Ala Arg 2775 2780 2785	8589
35	TGG TAT ACC AAA CTT GGA TTC TTT CCT GAC CCT AGA CCT TTT CCT CTG Trp Tyr Thr Lys Leu Gly Phe Phe Pro Asp Pro Arg Pro Phe Pro Leu 2790 2795 2800	8637
40	CCC TTA TCA TCG CTT TTC AGT GAT GGA GGA AAT GTT GGT TGT GTT GAT Pro Leu Ser Ser Leu Phe Ser Asp Gly Gly Asn Val Gly Cys Val Asp 2805 2810 2815	8685
45	GTA ATT ATT CAA AGA GCA TAC CCT ATA CAG TGG ATG GAG AAG ACA TCA Val Ile Ile Gln Arg Ala Tyr Pro Ile Gln Trp Met Glu Lys Thr Ser 2820 2825 2830 2835	8733
	TCT GGA TTA TAC ATA TTT CGC AAT GAA AGA GAG GAA GAA AAG GAA GCA Ser Gly Leu Tyr Ile Phe Arg Asn Glu Arg Glu Glu Glu Lys Glu Ala 2840 2845 2850	8781
50	GCA AAA TAT GTG GAG GCC CAA CAA AAG AGA CTA GAA GCC TTA TTC ACT Ala Lys Tyr Val Glu Ala Gln Gln Lys Arg Leu Glu Ala Leu Phe Thr 2855 2860 2865	8829
55	AAA ATT CAG GAG GAA TTT GAA GAA CAT GAA GAA AAC ACA ACA AAA CCA Lys Ile Gln Glu Glu Phe Glu Glu His Glu Glu Asn Thr Thr Lys Pro 2870 2875 2880	8877
60	TAT TTA CCA TCA CGT GCA CTA ACA AGA CAG CAA GTT CGT GCT TTG CAA Tyr Leu Pro Ser Arg Ala Leu Thr Arg Gln Gln Val Arg Ala Leu Gln 2885 2890 2895	8925
	GAT GGT GCA GAG CTT TAT GAA GCA GTG AAG AAT GCA GCA GAC CCA GCT	8973

	Asp Gly Ala Glu Leu Tyr Glu Ala Val Lys Asn Ala Ala Asp Pro Ala	
	2900 2905 2910 2915	
5	TAC CTT GAG GGT TAT TTC AGT GAA GAG CAG TTA AGA GCC TTG AAT AAT Tyr Leu Glu Gly Tyr Phe Ser Glu Glu Gln Leu Arg Ala Leu Asn Asn	9021
	2920 2925 2930	
10	CAC AGG CAA ATG TTG AAT GAT AAG AAA CAA GCT CAG ATC CAG TTG GAA His Arg Gln Met Leu Asn Asp Lys Lys Gln Ala Gln Ile Gln Leu Glu	9069
	2935 2940 2945	
15	ATT AGG AAG ACC ATG GAA TCT GCT GAA CAA AAG GAA CAA GGT TTA TCA Ile Arg Lys Thr Met Glu Ser Ala Glu Gln Lys Glu Gln Gly Leu Ser	9117
	2950 2955 2960	
20	AGG GAT GTC ACA ACC GTG TGG AAG TTG CGT ATT GTA AGC TAT TCA AAA Arg Asp Val Thr Thr Val Trp Lys Leu Arg Ile Val Ser Tyr Ser Lys	9165
	2965 2970 2975	
25	AAA GAA AAA GAT TCA GTT ATA CTG AGT ATT TGG CGT CCA TCA TCA GAT Lys Glu Lys Asp Ser Val Ile Leu Ser Ile Trp Arg Pro Ser Ser Asp	9213
	2980 2985 2990 2995	
30	TTA TAT TCT CTG TTA ACA GAA GGA AAG AGA TAC AGA ATT TAT CAT CTT Leu Tyr Ser Leu Leu Thr Glu Gly Lys Arg Tyr Arg Ile Tyr His Leu	9261
	3000 3005 3010	
35	GCA ACT TCA AAA TCT AAA AGT AAA TCT GAA AGA GCT AAC ATA CAG TTA Ala Thr Ser Lys Ser Lys Ser Lys Ser Glu Arg Ala Asn Ile Gln Leu	9309
	3015 3020 3025	
40	GCA GCG ACA AAA AAA ACT CAG TAT CAA CAA CTA CCG GTT TCA GAT GAA Ala Ala Thr Lys Lys Thr Gln Tyr Gln Gln Leu Pro Val Ser Asp Glu	9357
	3030 3035 3040	
45	ATT TTA TTT CAG ATT TAC CAG CCA CGG GAG CCC CTT CAC TTC AGC AAA Ile Leu Phe Gln Ile Tyr Gln Pro Arg Glu Pro Leu His Phe Ser Lys	9405
	3045 3050 3055	
50	TTT TTA GAT CCA GAC TTT CAG CCA TCT TGT TCT GAG GTG GAC CTA ATA Phe Leu Asp Pro Asp Phe Gln Pro Ser Cys Ser Glu Val Asp Leu Ile	9453
	3060 3065 3070 3075	
55	GGA TTT GTC GTT TCT GTT GTG AAA AAA ACA GGA CTT GCC CCT TTC GTC Gly Phe Val Val Ser Val Val Lys Lys Thr Gly Leu Ala Pro Phe Val	9501
	3080 3085 3090	
60	TAT TTG TCA GAC GAA TGT TAC AAT TTA CTG GCA ATA AAG TTT TGG ATA Tyr Leu Ser Asp Glu Cys Tyr Asn Leu Leu Ala Ile Lys Phe Trp Ile	9549
	3095 3100 3105	
65	GAC CTT AAT GAG GAC ATT ATT AAG CCT CAT ATG TTA ATT GCT GCA AGC Asp Leu Asn Glu Asp Ile Ile Lys Pro His Met Leu Ile Ala Ala Ser	9597
	3110 3115 3120	
70	AAC CTC CAG TGG CGA CCA GAA TCC AAA TCA GGC CTT CTT ACT TTA TTT Asn Leu Gln Trp Arg Pro Glu Ser Lys Ser Gly Leu Leu Thr Leu Phe	9645
	3125 3130 3135	
75	GCT GGA GAT TTT TCT GTG TTT TCT GCT AGT CCA AAA GAG GGC CAC TTT Ala Gly Asp Phe Ser Val Phe Ser Ala Ser Pro Lys Glu Gly His Phe	9693

	3140	3145	3150	3155	
5	CAA GAG ACA TTC AAC AAA ATG AAA AAT ACT GTT GAG AAT ATT GAC ATA Gln Glu Thr Phe Asn Lys Met Lys Asn Thr Val Glu Asn Ile Asp Ile	3160	3165	3170	9741
10	CTT TGC AAT GAA GCA GAA AAC AAG CTT ATG CAT ATA CTG CAT GCA AAT Leu Cys Asn Glu Ala Glu Asn Lys Leu Met His Ile Leu His Ala Asn	3175	3180	3185	9789
15	GAT CCC AAG TGG TCC ACC CCA ACT AAA GAC TGT ACT TCA GGG CCG TAC Asp Pro Lys Trp Ser Thr Pro Thr Lys Asp Cys Thr Ser Gly Pro Tyr	3190	3195	3200	9837
20	ACT GCT CAA ATC ATT CCT GGT ACA GGA AAC AAG CTT CTG ATG TCT TCT Thr Ala Gln Ile Ile Pro Gly Thr Gly Asn Lys Leu Leu Met Ser Ser	3205	3210	3215	9885
25	CCT AAT TGT GAG ATA TAT TAT CAA AGT CCT TTA TCA CTT TGT ATG GCC Pro Asn Cys Glu Ile Tyr Tyr Gln Ser Pro Leu Ser Leu Cys Met Ala	3220	3225	3230	9933
30	AAA AGG AAG TCT GTT TCC ACA CCT GTC TCA GCC CAG ATG ACT TCA AAG Lys Arg Lys Ser Val Ser Thr Pro Val Ser Ala Gln Met Thr Ser Lys	3240	3245	3250	9981
35	TCT TGT AAA GGG GAG AAA GAG ATT GAT GAC CAA AAG AAC TGC AAA AAG Ser Cys Lys Gly Glu Lys Glu Ile Asp Asp Gln Lys Asn Cys Lys Lys	3255	3260	3265	10029
40	AGA AGA GCC TTG GAT TTC TTG AGT AGA CTG CCT TTA CCT CCA CCT GTT Arg Arg Ala Leu Asp Phe Leu Ser Arg Leu Pro Leu Pro Pro Pro Val	3270	3275	3280	10077
45	AGT CCC ATT TGT ACA TTT GTT TCT CCG GCT GCA CAG AAG GCA TTT CAG Ser Pro Ile Cys Thr Phe Val Ser Pro Ala Ala Gln Lys Ala Phe Gln	3285	3290	3295	10125
50	CCA CCA AGG AGT TGT CGC ACC AAA TAC GAA ACA CCC ATA AAG AAA AAA Pro Pro Arg Ser Cys Gly Thr Lys Tyr Glu Thr Pro Ile Lys Lys Lys	3300	3305	3310	10173
55	GAA CTG AAT TCT CCT CAG ATG ACT CCA TTT AAA AAA TTC AAT GAA ATT Glu Leu Asn Ser Pro Gln Met Thr Pro Phe Lys Lys Phe Asn Glu Ile	3320	3325	3330	10221
60	TCT CTT TTG GAA AGT AAT TCA ATA GCT GAC GAA GAA CTT GCA TTG ATA Ser Leu Leu Glu Ser Asn Ser Ile Ala Asp Glu Glu Leu Ala Leu Ile	3335	3340	3345	10269
	AAT ACC CAA GCT CTT TTG TCT GGT TCA ACA GGA GAA AAA CAA TTT ATA Asn Thr Gln Ala Leu Leu Ser Gly Ser Thr Gly Glu Lys Gln Phe Ile	3350	3355	3360	10317
	TCT GTC AGT GAA TCC ACT AGG ACT GCT CCC ACC AGT TCA GAA GAT TAT Ser Val Ser Glu Ser Thr Arg Thr Ala Pro Thr Ser Ser Glu Asp Tyr	3365	3370	3375	10365
	CTC AGA CTG AAA CGA CGT TGT ACT ACA TCT CTG ATC AAA GAA CAG GAG Leu Arg Leu Lys Arg Arg Cys Thr Thr Ser Leu Ile Lys Glu Gln Glu	3380	3385	3390	10413



AGT TCC CAG GCC AGT ACG GAA GAA TGT GAG AAA AAT AAG CAG GAC ACA 10461  
 Ser Ser Gln Ala Ser Thr Glu Glu Cys Glu Lys Asn Lys Gln Asp Thr  
 5 3400 3405 3410

ATT ACA ACT AAA AAA TAT ATC TAA 10485  
 Ile Thr Thr Lys Lys Tyr Ile  
 3415

## (2) INFORMATION FOR SEQ ID NO:13:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 3418 amino acids  
 (B) TYPE: amino acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: protein

## (v) FRAGMENT TYPE: internal

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

25 Met Pro Ile Gly Ser Lys Glu Arg Pro Thr Phe Phe Glu Ile Phe Lys  
 1 5 10 15  
 Thr Arg Cys Asn Lys Ala Asp Leu Gly Pro Ile Ser Leu Asn Trp Phe  
 20 25 30  
 Glu Glu Leu Ser Ser Glu Ala Pro Tyr Asn Ser Glu Pro Ala Glu  
 30 35 40 45  
 Glu Ser Glu His Lys Asn Asn Asn Tyr Glu Pro Asn Leu Phe Lys Thr  
 50 55 60  
 Pro Gln Arg Lys Pro Ser Tyr Asn Gln Leu Ala Ser Thr Pro Ile Ile  
 65 70 75 80  
 35 Phe Lys Glu Gln Gly Leu Thr Leu Pro Leu Tyr Gln Ser Pro Val Lys  
 85 90 95  
 Glu Leu Asp Lys Phe Lys Leu Asp Leu Gly Arg Asn Val Pro Asn Ser  
 100 105 110  
 Arg His Lys Ser Leu Arg Thr Val Lys Thr Lys Met Asp Gln Ala Asp  
 115 120 125  
 40 Asp Val Ser Cys Pro Leu Leu Asn Ser Cys Leu Ser Glu Ser Pro Val  
 130 135 140  
 Val Leu Gln Cys Thr His Val Thr Pro Gln Arg Asp Lys Ser Val Val  
 145 150 155 160  
 45 Cys Gly Ser Leu Phe His Thr Pro Lys Phe Val Lys Gly Arg Gln Thr  
 165 170 175  
 Pro Lys His Ile Ser Glu Ser Leu Gly Ala Glu Val Asp Pro Asp Met  
 180 185 190  
 Ser Trp Ser Ser Ser Leu Ala Thr Pro Pro Thr Leu Ser Ser Thr Val  
 195 200 205  
 50 Leu Ile Val Arg Asn Glu Glu Ala Ser Glu Thr Val Phe Pro His Asp  
 210 215 220  
 Thr Thr Ala Asn Val Lys Ser Tyr Phe Ser Asn His Asp Glu Ser Leu  
 225 230 235 240  
 55 Lys Lys Asn Asp Arg Phe Ile Ala Ser Val Thr Asp Ser Glu Asn Thr  
 245 250 255  
 Asn Gln Arg Glu Ala Ala Ser His Gly Phe Gly Lys Thr Ser Gly Asn  
 260 265 270  
 Ser Phe Lys Val Asn Ser Cys Lys Asp His Ile Gly Lys Ser Met Pro  
 275 280 285  
 60 His Val Leu Glu Asp Glu Val Tyr Glu Thr Val Val Asp Thr Ser Glu  
 290 295 300

	Glu	Asp	Ser	Phe	Ser	Leu	Cys	Phe	Ser	Lys	Cys	Arg	Thr	Lys	Asn	Leu
	305					310					315					320
5	Gln	Lys	Val	Arg	Thr	Ser	Lys	Thr	Arg	Lys	Lys	Ile	Phe	His	Glu	Ala
					325					330					335	
	Asn	Ala	Asp	Glu	Cys	Glu	Lys	Ser	Lys	Asn	Gln	Val	Lys	Glu	Lys	Tyr
				340					345					350		
	Ser	Phe	Val	Ser	Glu	Val	Glu	Pro	Asn	Asp	Thr	Asp	Pro	Leu	Asp	Ser
			355					360					365			
10	Asn	Val	Ala	His	Gln	Lys	Pro	Phe	Glu	Ser	Gly	Ser	Asp	Lys	Ile	Ser
		370					375						380			
	Lys	Glu	Val	Val	Pro	Ser	Leu	Ala	Cys	Glu	Trp	Ser	Gln	Leu	Thr	Leu
	385					390					395					400
	Ser	Gly	Leu	Asn	Gly	Ala	Gln	Met	Glu	Lys	Ile	Pro	Leu	Leu	His	Ile
15				405						410					415	
	Ser	Ser	Cys	Asp	Gln	Asn	Ile	Ser	Glu	Lys	Asp	Leu	Leu	Asp	Thr	Glu
				420					425					430		
	Asn	Lys	Arg	Lys	Lys	Asp	Phe	Leu	Thr	Ser	Glu	Asn	Ser	Leu	Pro	Arg
			435					440					445			
20	Ile	Ser	Ser	Leu	Pro	Lys	Ser	Glu	Lys	Pro	Leu	Asn	Glu	Glu	Thr	Val
		450					455						460			
	Val	Asn	Lys	Arg	Asp	Glu	Gln	His	Leu	Glu	Ser	His	Thr	Asp	Cys	
	465					470				475					480	
	Ile	Leu	Ala	Val	Lys	Gln	Ala	Ile	Ser	Gly	Thr	Ser	Pro	Val	Ala	Ser
25					485					490					495	
	Ser	Phe	Gln	Gly	Ile	Lys	Lys	Ser	Ile	Phe	Arg	Ile	Arg	Glu	Ser	Pro
				500					505					510		
	Lys	Glu	Thr	Phe	Asn	Ala	Ser	Phe	Ser	Gly	His	Met	Thr	Asp	Pro	Asn
		515						520					525			
30	Phe	Lys	Lys	Glu	Thr	Glu	Ala	Ser	Glu	Ser	Gly	Leu	Glu	Ile	His	Thr
		530					535					540				
	Val	Cys	Ser	Gln	Lys	Glu	Asp	Ser	Leu	Cys	Pro	Asn	Leu	Ile	Asp	Asn
	545					550					555					560
	Gly	Ser	Trp	Pro	Ala	Thr	Thr	Thr	Gln	Asn	Ser	Val	Ala	Leu	Lys	Asn
35					565					570					575	
	Ala	Gly	Leu	Ile	Ser	Thr	Leu	Lys	Lys	Thr	Asn	Lys	Phe	Ile	Tyr	
				580					585				590			
	Ala	Ile	His	Asp	Glu	Thr	Ser	Tyr	Lys	Gly	Lys	Lys	Ile	Pro	Lys	Asp
			595					600					605			
40	Gln	Lys	Ser	Glu	Leu	Ile	Asn	Cys	Ser	Ala	Gln	Phe	Glu	Ala	Asn	Ala
		610					615					620				
	Phe	Glu	Ala	Pro	Leu	Thr	Phe	Ala	Asn	Ala	Asp	Ser	Gly	Leu	Leu	His
	625					630					635					640
	Ser	Ser	Val	Lys	Arg	Ser	Cys	Ser	Gln	Asn	Asp	Ser	Glu	Glu	Pro	Thr
45					645					650					655	
	Leu	Ser	Leu	Thr	Ser	Ser	Phe	Gly	Thr	Ile	Leu	Arg	Lys	Cys	Ser	Arg
				660					665					670		
	Asn	Glu	Thr	Cys	Ser	Asn	Asn	Thr	Val	Ile	Ser	Gln	Asp	Leu	Asp	Tyr
		675						680					685			
50	Lys	Glu	Ala	Lys	Cys	Asn	Lys	Glu	Lys	Leu	Gln	Leu	Phe	Ile	Thr	Pro
		690					695					700				
	Glu	Ala	Asp	Ser	Leu	Ser	Cys	Leu	Gln	Glu	Gly	Gln	Cys	Glu	Asn	Asp
	705					710					715				720	
	Pro	Lys	Ser	Lys	Lys	Val	Ser	Asp	Ile	Lys	Glu	Glu	Val	Leu	Ala	Ala
55					725					730					735	
	Ala	Cys	His	Pro	Val	Gln	His	Ser	Lys	Val	Glu	Tyr	Ser	Asp	Thr	Asp
				740					745					750		
	Phe	Gln	Ser	Gln	Lys	Ser	Leu	Leu	Tyr	Asp	His	Glu	Asn	Ala	Ser	Thr
			755					760					765			
60	Leu	Ile	Leu	Thr	Pro	Thr	Ser	Lys	Asp	Val	Leu	Ser	Asn	Leu	Val	Met
		770					775					780				
	Ile	Ser	Arg	Gly	Lys	Glu	Ser	Tyr	Lys	Met	Ser	Asp	Lys	Leu	Lys	Gly

	785				790				795				800			
	Asn	Asn	Tyr	Glu	Ser	Asp	Val	Glu	Leu	Thr	Lys	Asn	Ile	Pro	Met	Glu
					805				810							815
5	Lys	Asn	Gln	Asp	Val	Cys	Ala	Leu	Asn	Glu	Asn	Tyr	Lys	Asn	Val	Glu
				820					825					830		
	Leu	Leu	Pro	Pro	Glu	Lys	Tyr	Met	Arg	Val	Ala	Ser	Pro	Ser	Arg	Lys
				835					840					845		
10	Val	Gln	Phe	Asn	Gln	Asn	Thr	Asn	Leu	Arg	Val	Ile	Gln	Lys	Asn	Gln
		850					855					860				
	Glu	Glu	Thr	Thr	Ser	Ile	Ser	Lys	Ile	Thr	Val	Asn	Pro	Asp	Ser	Glu
						870					875					880
	Glu	Leu	Phe	Ser	Asp	Asn	Glu	Asn	Asn	Phe	Val	Phe	Gln	Ile	Ala	Asn
					885					890						895
15	Glu	Arg	Asn	Asn	Leu	Ala	Leu	Gly	Asn	Thr	Lys	Glu	Leu	His	Glu	Thr
				900					905					910		
	Asp	Leu	Thr	Cys	Val	Asn	Glu	Pro	Ile	Phe	Lys	Asn	Ser	Thr	Met	Val
				915				920					925			
20	Leu	Tyr	Gly	Asp	Thr	Gly	Asp	Lys	Gln	Ala	Thr	Ala	Val	Ser	Ile	Lys
		930					935						940			
	Lys	Asp	Leu	Val	Tyr	Val	Leu	Ala	Glu	Glu	Asn	Lys	Asn	Ser	Val	Lys
		945				950					955					960
	Gln	His	Ile	Lys	Met	Thr	Leu	Gly	Gln	Asp	Leu	Lys	Ser	Asp	Ile	Ser
				965						970					975	
25	Leu	Asn	Ile	Asp	Lys	Ile	Pro	Glu	Lys	Asn	Asn	Asp	Tyr	Met	Asp	Lys
				980					985					990		
	Trp	Ala	Gly	Leu	Leu	Gly	Pro	Ile	Ser	Asn	His	Ser	Phe	Gly	Gly	Ser
			995					1000						1005		
30	Phe	Arg	Thr	Ala	Ser	Asn	Lys	Glu	Ile	Lys	Leu	Ser	Glu	His	Asn	Ile
		1010					1015						1020			
	Lys	Lys	Ser	Lys	Met	Phe	Phe	Lys	Asp	Ile	Glu	Glu	Gln	Tyr	Pro	Thr
						1030					1035					104
	Ser	Leu	Ala	Cys	Val	Glu	Ile	Val	Asn	Thr	Leu	Ala	Leu	Asp	Asn	Gln
				1045						1050					1055	
35	Lys	Lys	Leu	Ser	Lys	Pro	Gln	Ser	Ile	Asn	Thr	Val	Ser	Ala	His	Leu
				1060					1065					1070		
	Gln	Ser	Ser	Val	Val	Val	Ser	Asp	Cys	Lys	Asn	Ser	His	Ile	Thr	Pro
			1075					1080					1085			
40	Gln	Met	Leu	Phe	Ser	Lys	Gln	Asp	Phe	Asn	Ser	Asn	His	Asn	Leu	Thr
		1090					1095						1100			
	Pro	Ser	Gln	Lys	Ala	Glu	Ile	Thr	Glu	Leu	Ser	Thr	Ile	Leu	Glu	Glu
						1110					1115					112
	Ser	Gly	Ser	Gln	Phe	Glu	Phe	Thr	Gln	Phe	Arg	Lys	Pro	Ser	Tyr	Ile
				1125						1130					1135	
45	Leu	Gln	Lys	Ser	Thr	Phe	Glu	Val	Pro	Glu	Asn	Gln	Met	Thr	Ile	Leu
				1140					1145					1150		
	Lys	Thr	Thr	Ser	Glu	Glu	Cys	Arg	Asp	Ala	Asp	Leu	His	Val	Ile	Met
			1155					1160					1165			
50	Asn	Ala	Pro	Ser	Ile	Gly	Gln	Val	Asp	Ser	Ser	Lys	Gln	Phe	Glu	Gly
		1170					1175					1180				
	Thr	Val	Glu	Ile	Lys	Arg	Lys	Phe	Ala	Gly	Leu	Leu	Lys	Asn	Asp	Cys
						1190				1195						120
	Asn	Lys	Ser	Ala	Ser	Gly	Tyr	Leu	Thr	Asp	Glu	Asn	Glu	Val	Gly	Phe
				1205						1210					1215	
55	Arg	Gly	Phe	Tyr	Ser	Ala	His	Gly	Thr	Lys	Leu	Asn	Val	Ser	Thr	Glu
				1220					1225					1230		
	Ala	Leu	Gln	Lys	Ala	Val	Lys	Leu	Phe	Ser	Asp	Ile	Glu	Asn	Ile	Ser
				1235				1240				1245				
	Glu	Glu	Thr	Ser	Ala	Glu	Val	His	Pro	Ile	Ser	Leu	Ser	Ser	Ser	Lys
		1250					1255					1260				
60	Cys	His	Asp	Ser	Val	Val	Ser	Met	Phe	Lys	Ile	Glu	Asn	His	Asn	Asp
						1270					1275					128

Lys Thr Val Ser Glu Lys Asn Asn Lys Cys Gln Leu Ile Leu Gln Asn  
 1285 1290 1295  
 Asn Ile Glu Met Thr Thr Gly Thr Phe Val Glu Glu Ile Thr Glu Asn  
 1300 1305 1310  
 5 Tyr Lys Arg Asn Thr Glu Asn Glu Asp Asn Lys Tyr Thr Ala Ala Ser  
 1315 1320 1325  
 Arg Asn Ser His Asn Leu Glu Phe Asp Gly Ser Asp Ser Ser Lys Asn  
 1330 1335 1340  
 10 Asp Thr Val Cys Ile His Lys Asp Glu Thr Asp Leu Leu Phe Thr Asp  
 1345 1350 1355 136  
 Gln His Asn Ile Cys Leu Lys Leu Ser Gly Gln Phe Met Lys Glu Gly  
 1365 1370 1375  
 Asn Thr Gln Ile Lys Glu Asp Leu Ser Asp Leu Thr Phe Leu Glu Val  
 1380 1385 1390  
 15 Ala Lys Ala Gln Glu Ala Cys His Gly Asn Thr Ser Asn Lys Glu Gln  
 1395 1400 1405  
 Leu Thr Ala Thr Lys Thr Glu Gln Asn Ile Lys Asp Phe Glu Thr Ser  
 1410 1415 1420  
 20 Asp Thr Phe Phe Gln Thr Ala Ser Gly Lys Asn Ile Ser Val Ala Lys  
 1425 1430 1435 144  
 Glu Ser Phe Asn Lys Ile Val Asn Phe Phe Asp Gln Lys Pro Glu Glu  
 1445 1450 1455  
 Leu His Asn Phe Ser Leu Asn Ser Glu Leu His Ser Asp Ile Arg Lys  
 1460 1465 1470  
 25 Asn Lys Met Asp Ile Leu Ser Tyr Glu Glu Thr Asp Ile Val Lys His  
 1475 1480 1485  
 Lys Ile Leu Lys Glu Ser Val Pro Val Gly Thr Gly Asn Gln Leu Val  
 1490 1495 1500  
 30 Thr Phe Gln Gly Gln Pro Glu Arg Asp Glu Lys Ile Lys Glu Pro Thr  
 1505 1510 1515 152  
 Leu Leu Gly Phe His Thr Ala Ser Gly Lys Lys Val Lys Ile Ala Lys  
 1525 1530 1535  
 Glu Ser Leu Asp Lys Val Lys Asn Leu Phe Asp Glu Lys Glu Gln Gly  
 1540 1545 1550  
 35 Thr Ser Glu Ile Thr Ser Phe Ser His Gln Trp Ala Lys Thr Leu Lys  
 1555 1560 1565  
 Tyr Arg Glu Ala Cys Lys Asp Leu Glu Leu Ala Cys Glu Thr Ile Glu  
 1570 1575 1580  
 40 Ile Thr Ala Ala Pro Lys Cys Lys Glu Met Gln Asn Ser Leu Asn Asn  
 1585 1590 1595 160  
 Asp Lys Asn Leu Val Ser Ile Glu Thr Val Val Pro Pro Lys Leu Leu  
 1605 1610 1615  
 Ser Asp Asn Leu Cys Arg Gln Thr Glu Asn Leu Lys Thr Ser Lys Ser  
 1620 1625 1630  
 45 Ile Phe Leu Lys Val Lys Val His Glu Asn Val Glu Lys Glu Thr Ala  
 1635 1640 1645  
 Lys Ser Pro Ala Thr Cys Tyr Thr Asn Gln Ser Pro Tyr Ser Val Ile  
 1650 1655 1660  
 50 Glu Asn Ser Ala Leu Ala Phe Tyr Thr Ser Cys Ser Arg Lys Thr Ser  
 1665 1670 1675 168  
 Val Ser Gln Thr Ser Leu Leu Glu Ala Lys Lys Trp Leu Arg Glu Gly  
 1685 1690 1695  
 Ile Phe Asp Gly Gln Pro Glu Arg Ile Asn Thr Ala Asp Tyr Val Gly  
 1700 1705 1710  
 55 Asn Tyr Leu Tyr Glu Asn Asn Ser Asn Ser Thr Ile Ala Glu Asn Asp  
 1715 1720 1725  
 Lys Asn His Leu Ser Glu Lys Gln Asp Thr Tyr Leu Ser Asn Ser Ser  
 1730 1735 1740  
 60 Met Ser Asn Ser Tyr Ser Tyr His Ser Asp Glu Val Tyr Asn Asp Ser  
 1745 1750 1755 176  
 Gly Tyr Leu Ser Lys Asn Lys Leu Asp Ser Gly Ile Glu Pro Val Leu

	1765	1770	1775
	Lys Asn Val Glu Asp Gln	Lys Asn Thr Ser Phe Ser	Lys Val Ile Ser
	1780	1785	1790
5	Asn Val Lys Asp Ala Asn Ala Tyr Pro Gln Thr Val Asn Glu Asp Ile		
	1795	1800	1805
	Cys Val Glu Glu Leu Val Thr Ser Ser Ser Pro Cys Lys Asn Lys Asn		
	1810	1815	1820
10	Ala Ala Ile Lys Leu Ser Ile Ser Asn Ser Asn Asn Phe Glu Val Gly		
	1825	1830	1835
	Pro Pro Ala Phe Arg Ile Ala Ser Gly Lys Ile Val Cys Val Ser His		
	1845	1850	1855
	Glu Thr Ile Lys Lys Val Lys Asp Ile Phe Thr Asp Ser Phe Ser Lys		
	1860	1865	1870
15	Val Ile Lys Glu Asn Asn Glu Asn Lys Ser Lys Ile Cys Gln Thr Lys		
	1875	1880	1885
	Ile Met Ala Gly Cys Tyr Glu Ala Leu Asp Asp Ser Glu Asp Ile Leu		
	1890	1895	1900
20	His Asn Ser Leu Asp Asn Asp Glu Cys Ser Thr His Ser His Lys Val		
	1905	1910	1915
	Phe Ala Asp Ile Gln Ser Glu Glu Ile Leu Gln His Asn Gln Asn Met		
	1925	1930	1935
	Ser Gly Leu Glu Lys Val Ser Lys Ile Ser Pro Cys Asp Val Ser Leu		
	1940	1945	1950
25	Glu Thr Ser Asp Ile Cys Lys Cys Ser Ile Gly Lys Leu His Lys Ser		
	1955	1960	1965
	Val Ser Ser Ala Asn Thr Cys Gly Ile Phe Ser Thr Ala Ser Gly Lys		
	1970	1975	1980
30	Ser Val Gln Val Ser Asp Ala Ser Leu Gln Asn Ala Arg Gln Val Phe		
	1985	1990	1995
	Ser Glu Ile Glu Asp Ser Thr Lys Gln Val Phe Ser Lys Val Leu Phe		
	2005	2010	2015
	Lys Ser Asn Glu His Ser Asp Gln Leu Thr Arg Glu Glu Asn Thr Ala		
	2020	2025	2030
35	Ile Arg Thr Pro Glu His Leu Ile Ser Gln Lys Gly Phe Ser Tyr Asn		
	2035	2040	2045
	Val Val Asn Ser Ser Ala Phe Ser Gly Phe Ser Thr Ala Ser Gly Lys		
	2050	2055	2060
40	Gln Val Ser Ile Leu Glu Ser Ser Leu His Lys Val Lys Gly Val Leu		
	2065	2070	2075
	Glu Glu Phe Asp Leu Ile Arg Thr Glu His Ser Leu His Tyr Ser Pro		
	2085	2090	2095
	Thr Ser Arg Gln Asn Val Ser Lys Ile Leu Pro Arg Val Asp Lys Arg		
	2100	2105	2110
45	Asn Pro Glu His Cys Val Asn Ser Glu Met Glu Lys Thr Cys Ser Lys		
	2115	2120	2125
	Glu Phe Lys Leu Ser Asn Asn Leu Asn Val Glu Gly Gly Ser Ser Glu		
	2130	2135	2140
50	Asn Asn His Ser Ile Lys Val Ser Pro Tyr Leu Ser Gln Phe Gln Gln		
	2145	2150	2155
	Asp Lys Gln Gln Leu Val Leu Gly Thr Lys Val Ser Leu Val Glu Asn		
	2165	2170	2175
	Ile His Val Leu Gly Lys Glu Gln Ala Ser Pro Lys Asn Val Lys Met		
	2180	2185	2190
55	Glu Ile Gly Lys Thr Glu Thr Phe Ser Asp Val Pro Val Lys Thr Asn		
	2195	2200	2205
	Ile Glu Val Cys Ser Thr Tyr Ser Lys Asp Ser Glu Asn Tyr Phe Glu		
	2210	2215	2220
60	Thr Glu Ala Val Glu Ile Ala Lys Ala Phe Met Glu Asp Asp Glu Leu		
	2225	2230	2235
	Thr Asp Ser Lys Leu Pro Ser His Ala Thr His Ser Leu Phe Thr Cys		
	2245	2250	2255

Pro Glu Asn Glu Glu Met Val Leu Ser Asn Ser Arg Ile Gly Lys Arg  
 2260 2265 2270  
 5 Arg Gly Glu Pro Leu Ile Leu Val Gly Glu Pro Ser Ile Lys Arg Asn  
 2275 2280 2285  
 Leu Leu Asn Glu Phe Asp Arg Ile Ile Glu Asn Gln Glu Lys Ser Leu  
 2290 2295 2300  
 Lys Ala Ser Lys Ser Thr Pro Asp Gly Thr Ile Lys Asp Arg Arg Leu  
 2305 2310 2315 232  
 10 Phe Met His His Val Ser Leu Glu Pro Ile Thr Cys Val Pro Phe Arg  
 2325 2330 2335  
 Thr Thr Lys Glu Arg Gln Glu Ile Gln Asn Pro Asn Phe Thr Ala Pro  
 2340 2345 2350  
 15 Gly Gln Glu Phe Leu Ser Lys Ser His Leu Tyr Glu His Leu Thr Leu  
 2355 2360 2365  
 Glu Lys Ser Ser Ser Asn Leu Ala Val Ser Gly His Pro Phe Tyr Gln  
 2370 2375 2380  
 Val Ser Ala Thr Arg Asn Glu Lys Met Arg His Leu Ile Thr Thr Gly  
 2385 2390 2395 240  
 20 Arg Pro Thr Lys Val Phe Val Pro Pro Phe Lys Thr Lys Ser His Phe  
 2405 2410 2415  
 His Arg Val Glu Gln Cys Val Arg Asn Ile Asn Leu Glu Glu Asn Arg  
 2420 2425 2430  
 25 Gln Lys Gln Asn Ile Asp Gly His Gly Ser Asp Asp Ser Lys Asn Lys  
 2435 2440 2445  
 Ile Asn Asp Asn Glu Ile His Gln Phe Asn Lys Asn Asn Ser Asn Gln  
 2450 2455 2460  
 Ala Ala Ala Val Thr Phe Thr Lys Cys Glu Glu Pro Leu Asp Leu  
 2465 2470 2475 248  
 30 Ile Thr Ser Leu Gln Asn Ala Arg Asp Ile Gln Asp Met Arg Ile Lys  
 2485 2490 2495  
 Lys Lys Gln Arg Gln Arg Val Phe Pro Gln Pro Gly Ser Leu Tyr Leu  
 2500 2505 2510  
 35 Ala Lys Thr Ser Thr Leu Pro Arg Ile Ser Leu Lys Ala Ala Val Gly  
 2515 2520 2525  
 Gly Gln Val Pro Ser Ala Cys Ser His Lys Gln Leu Tyr Thr Tyr Gly  
 2530 2535 2540  
 Val Ser Lys His Cys Ile Lys Ile Asn Ser Lys Asn Ala Glu Ser Phe  
 2545 2550 2555 256  
 40 Gln Phe His Thr Glu Asp Tyr Phe Gly Lys Glu Ser Leu Trp Thr Gly  
 2565 2570 2575  
 Lys Gly Ile Gln Leu Ala Asp Gly Gly Trp Leu Ile Pro Ser Asn Asp  
 2580 2585 2590  
 45 Gly Lys Ala Gly Lys Glu Glu Phe Tyr Arg Ala Leu Cys Asp Thr Pro  
 2595 2600 2605  
 Gly Val Asp Pro Lys Leu Ile Ser Arg Ile Trp Val Tyr Asn His Tyr  
 2610 2615 2620  
 Arg Trp Ile Ile Trp Lys Leu Ala Ala Met Glu Cys Ala Phe Pro Lys  
 2625 2630 2635 264  
 50 Glu Phe Ala Asn Arg Cys Leu Ser Pro Glu Arg Val Leu Leu Gln Leu  
 2645 2650 2655  
 Lys Tyr Arg Tyr Asp Thr Glu Ile Asp Arg Ser Arg Arg Ser Ala Ile  
 2660 2665 2670  
 55 Lys Lys Ile Met Glu Arg Asp Asp Thr Ala Ala Lys Thr Leu Val Leu  
 2675 2680 2685  
 Cys Val Ser Asp Ile Ile Ser Leu Ser Ala Asn Ile Ser Glu Thr Ser  
 2690 2695 2700  
 Ser Asn Lys Thr Ser Ser Ala Asp Thr Gln Lys Val Ala Ile Ile Glu  
 2705 2710 2715 272  
 60 Leu Thr Asp Gly Trp Tyr Ala Val Lys Ala Gln Leu Asp Pro Pro Leu  
 2725 2730 2735  
 Leu Ala Val Leu Lys Asn Gly Arg Leu Thr Val Gly Gln Lys Ile Ile

		2740				2745				2750					
		Leu His Gly Ala Glu Leu Val Gly Ser Pro Asp Ala Cys Thr Pro Leu													
		2755				2760				2765					
5		Glu Ala Pro Glu Ser Leu Met Leu Lys Ile Ser Ala Asn Ser Thr Arg													
		2770				2775				2780					
		Pro Ala Arg Trp Tyr Thr Lys Leu Gly Phe Phe Pro Asp Pro Arg Pro													
		2785				2790				2795					280
		Phe Pro Leu Pro Leu Ser Ser Leu Phe Ser Asp Gly Gly Asn Val Gly													
10					2805				2810					2815	
		Cys Val Asp Val Ile Ile Gln Arg Ala Tyr Pro Ile Gln Trp Met Glu													
					2820				2825					2830	
		Lys Thr Ser Ser Gly Leu Tyr Ile Phe Arg Asn Glu Arg Glu Glu Glu													
					2835				2840					2845	
15		Lys Glu Ala Ala Lys Tyr Val Glu Ala Gln Gln Lys Arg Leu Glu Ala													
					2850				2855					2860	
		Leu Phe Thr Lys Ile Gln Glu Glu Phe Glu Glu His Glu Glu Asn Thr													
					2865				2870					2875	288
		Thr Lys Pro Tyr Leu Pro Ser Arg Ala Leu Thr Arg Gln Gln Val Arg													
20					2885				2890					2895	
		Ala Leu Gln Asp Gly Ala Glu Leu Tyr Glu Ala Val Lys Asn Ala Ala													
					2900				2905					2910	
		Asp Pro Ala Tyr Leu Glu Gly Tyr Phe Ser Glu Glu Gln Leu Arg Ala													
					2915				2920					2925	
25		Leu Asn Asn His Arg Gln Met Leu Asn Asp Lys Lys Gln Ala Gln Ile													
					2930				2935					2940	
		Gln Leu Glu Ile Arg Lys Thr Met Glu Ser Ala Glu Gln Lys Glu Gln													
					2945				2950					2955	296
		Gly Leu Ser Arg Asp Val Thr Thr Val Trp Lys Leu Arg Ile Val Ser													
30					2965				2970					2975	
		Tyr Ser Lys Lys Glu Lys Asp Ser Val Ile Leu Ser Ile Trp Arg Pro													
					2980				2985					2990	
		Ser Ser Asp Leu Tyr Ser Leu Leu Thr Glu Gly Lys Arg Tyr Arg Ile													
					2995				3000					3005	
35		Tyr His Leu Ala Thr Ser Lys Ser Lys Ser Lys Ser Glu Arg Ala Asn													
					3010				3015					3020	
		Ile Gln Leu Ala Ala Thr Lys Lys Thr Gln Tyr Gln Gln Leu Pro Val													
					3025				3030					3035	304
		Ser Asp Glu Ile Leu Phe Gln Ile Tyr Gln Pro Arg Glu Pro Leu His													
40					3045				3050					3055	
		Phe Ser Lys Phe Leu Asp Pro Asp Phe Gln Pro Ser Cys Ser Glu Val													
					3060				3065					3070	
		Asp Leu Ile Gly Phe Val Val Ser Val Val Lys Lys Thr Gly Leu Ala													
					3075				3080					3085	
45		Pro Phe Val Tyr Leu Ser Asp Glu Cys Tyr Asn Leu Leu Ala Ile Lys													
					3090				3095					3100	
		Phe Trp Ile Asp Leu Asn Glu Asp Ile Ile Lys Pro His Met Leu Ile													
					3105				3110					3115	312
		Ala Ala Ser Asn Leu Gln Trp Arg Pro Glu Ser Lys Ser Gly Leu Leu													
50					3125				3130					3135	
		Thr Leu Phe Ala Gly Asp Phe Ser Val Phe Ser Ala Ser Pro Lys Glu													
					3140				3145					3150	
		Gly His Phe Gln Glu Thr Phe Asn Lys Met Lys Asn Thr Val Glu Asn													
					3155				3160					3165	
55		Ile Asp Ile Leu Cys Asn Glu Ala Glu Asn Lys Leu Met His Ile Leu													
					3170				3175					3180	
		His Ala Asn Asp Pro Lys Trp Ser Thr Pro Thr Lys Asp Cys Thr Ser													
					3185				3190					3195	320
		Gly Pro Tyr Thr Ala Gln Ile Ile Pro Gly Thr Gly Asn Lys Leu Leu													
60					3205				3210					3215	
		Met Ser Ser Pro Asn Cys Glu Ile Tyr Tyr Gln Ser Pro Leu Ser Leu													
					3220				3225					3230	

Cys Met Ala Lys Arg Lys Ser Val Ser Thr Pro Val Ser Ala Gln Met  
 3235 3240 3245  
 5 Thr Ser Lys Ser Cys Lys Gly Glu Lys Glu Ile Asp Asp Gln Lys Asn  
 3250 3255 3260  
 Cys Lys Lys Arg Arg Ala Leu Asp Phe Leu Ser Arg Leu Pro Leu Pro  
 3265 3270 3275 328  
 Pro Pro Val Ser Pro Ile Cys Thr Phe Val Ser Pro Ala Ala Gln Lys  
 3285 3290 3295  
 10 Ala Phe Gln Pro Pro Arg Ser Cys Gly Thr Lys Tyr Glu Thr Pro Ile  
 3300 3305 3310  
 Lys Lys Lys Glu Leu Asn Ser Pro Gln Met Thr Pro Phe Lys Lys Phe  
 3315 3320 3325  
 Asn Glu Ile Ser Leu Leu Glu Ser Asn Ser Ile Ala Asp Glu Glu Leu  
 3330 3335 3340  
 15 Ala Leu Ile Asn Thr Gln Ala Leu Leu Ser Gly Ser Thr Gly Glu Lys  
 3345 3350 3355 336  
 Gln Phe Ile Ser Val Ser Glu Ser Thr Arg Thr Ala Pro Thr Ser Ser  
 3365 3370 3375  
 20 Glu Asp Tyr Leu Arg Leu Lys Arg Arg Cys Thr Thr Ser Leu Ile Lys  
 3380 3385 3390  
 Glu Gln Glu Ser Ser Gln Ala Ser Thr Glu Glu Cys Glu Lys Asn Lys  
 3395 3400 3405  
 25 Gln Asp Thr Ile Thr Thr Lys Lys Tyr Ile  
 3410 3415

## (2) INFORMATION FOR SEQ ID NO:14:

## (i) SEQUENCE CHARACTERISTICS:

- 30 (A) LENGTH: 20 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

35

- (A) NAME/KEY:  
 (B) LOCATION:  
 (D) OTHER INFORMATION: 2F primer

## 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

TGAGTTTAC CTCAGTCACA

20

## (2) INFORMATION FOR SEQ ID NO:16:

45

## (i) SEQUENCE CHARACTERISTICS:

- 50 (A) LENGTH: 41 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

55 CAGGAAACAG CTATGACCCT GTGACGTACT GGGTTTTTAG C

41

## (2) INFORMATION FOR SEQ ID NO:17:

## (i) SEQUENCE CHARACTERISTICS:

- 60 (A) LENGTH: 24 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single



(D) TOPOLOGY: linear

- 5 (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 3FII primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

10 GATCTTTAAC TGTTCCTGGGT CACA 24

(2) INFORMATION FOR SEQ ID NO:18:

- 15 (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 22 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

20

- (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 3RII primer

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

CCCAGCATGA CACAATTAAT GA 22

30 (2) INFORMATION FOR SEQ ID NO:19:

- (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 44 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

35

- (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 4F/M 13F primer

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

45 TGTAAACGA CGGCCAGTAG AATGCAAATT TATAATCCAG AGTA 44

(2) INFORMATION FOR SEQ ID NO:20:

- (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 22 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

50

55

- (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 4R-1A primer

60 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

ATCAGATTCA TCTTTATAGA AC 22

## (2) INFORMATION FOR SEQ ID NO:21:

## 5 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 40 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

10

(A) NAME/KEY:

(B) LOCATION:

(D) OTHER INFORMATION: 5+6F/M13F primer

15

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

TGTAACACGA CGGCCAGTTG TGTTGGCATT TTAAACATCA

40

20

## (2) INFORMATION FOR SEQ ID NO:22:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 38 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

25

(A) NAME/KEY:

(B) LOCATION:

(D) OTHER INFORMATION: 5+6R/M13R primer

30

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

35 CAGGAAACAG CTATGACCCA GGGCAAAGGT ATAACGCT

38

## (2) INFORMATION FOR SEQ ID NO:23:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 38 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

40

45

(A) NAME/KEY:

(B) LOCATION:

(D) OTHER INFORMATION: 7F/M13F primer

50

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

TGTAACACGA CGGCCAGTTA AGTGAAATAA AGAGTGAA

38

## (2) INFORMATION FOR SEQ ID NO:24:

55

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 36 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

60

(A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 7R/M13R primer

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:  
CAGGAAACAG CTATGACCAG AAGTATTAGA GATGAC 36

10 (2) INFORMATION FOR SEQ ID NO:25:  
(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 40 base pairs  
(B) TYPE: nucleic acid  
15 (C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(A) NAME/KEY:  
20 (B) LOCATION:  
(D) OTHER INFORMATION: 8F/M13F primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:  
25 TGTA AACGA CGGCCAGTGC CATATCTTAC CACCTTGTGA 40

(2) INFORMATION FOR SEQ ID NO:26:  
(i) SEQUENCE CHARACTERISTICS:  
30 (A) LENGTH: 22 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

35 (ix) FEATURE:  
(A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 8FIA primer

40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:  
TTGCATTCTA GTGATAATAT AC 22

45 (2) INFORMATION FOR SEQ ID NO:27:  
(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 19 base pairs  
(B) TYPE: nucleic acid  
50 (C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(A) NAME/KEY:  
55 (B) LOCATION:  
(D) OTHER INFORMATION: 8RIA primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:  
60 AATTGTTAGC AATTTCAAC 19

(2) INFORMATION FOR SEQ ID NO:28:

(i) SEQUENCE CHARACTERISTICS:  
5 (A) LENGTH: 40 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

10 (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 9F/M13F primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:  
15 TGTAAAACGA CGGCCAGTTG GACCTAGGTT GATTGCAGAT 40

(2) INFORMATION FOR SEQ ID NO:29:

20 (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 40 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

25 (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 9R/M13R primer

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:  
CAGGAAACAG CTATGACCTA AACTGAGATC ACGGGTGACA 40

(2) INFORMATION FOR SEQ ID NO:30:

35 (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 24 base pairs  
(B) TYPE: nucleic acid  
40 (C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(A) NAME/KEY:  
45 (B) LOCATION:  
(D) OTHER INFORMATION: 10AF primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:  
50 GAATAATATA AATTATATGG CTTA 24

(2) INFORMATION FOR SEQ ID NO:31:

55 (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 37 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

60 (A) NAME/KEY:  
(B) LOCATION:

(D) OTHER INFORMATION: 10AR/M13R primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:31:

5

CAGGAAACAG CTATGACCCC TAGTCTTGCT AGTTCTT

37

(2) INFORMATION FOR SEQ ID NO:32:

10

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 42 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

15

(A) NAME/KEY:

(B) LOCATION:

(D) OTHER INFORMATION: 10BF/M13F primer

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:

TGTAAAACGA CGGCCAGTAR CTGAAGTGA ACCAAATGAT AC

42

25

(2) INFORMATION FOR SEQ ID NO:33:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 44 base pairs

(B) TYPE: nucleic acid

30

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(A) NAME/KEY:

35

(B) LOCATION:

(D) OTHER INFORMATION: 10BR/M13R primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:

40

CAGGAAACAG CTATGACCAC GTGGCAAAGA ATTCTCTGAA GTAA

44

(2) INFORMATION FOR SEQ ID NO:34:

(i) SEQUENCE CHARACTERISTICS:

45

(A) LENGTH: 40 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

50

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(D) OTHER INFORMATION: 10CF/M13F primer

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:34:

TGTAAAACGA CGGCCAGTCA GCATCTTGAA TCTCATACAG

40

60

(2) INFORMATION FOR SEQ ID NO:35:

(i) SEQUENCE CHARACTERISTICS:

5 (A) LENGTH: 19 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

10 (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 10CRII primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:35:

15 AGACAGAGGT ACCTGAATC

19

(2) INFORMATION FOR SEQ ID NO:36:

20 (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 40 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

25 (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 11AF-M13 primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:

30 TGTAACACGA CGGCCAGTTG GTACTTTAAT TTTGTCACTT

40

(2) INFORMATION FOR SEQ ID NO:37:

35 (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 37 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

40

(A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 11AR-M13 primer

45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:

CAGGAAACAG CTATGACCTG CAGGCATGAC AGAGAAT

37

50 (2) INFORMATION FOR SEQ ID NO:38:

55 (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 22 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

60 (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 11BF primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:38:

AAGAAGCAAA ATGTAATAAG GA

22

5

(2) INFORMATION FOR SEQ ID NO:39:

(i) SEQUENCE CHARACTERISTICS:

10

- (A) LENGTH: 22 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

15

- (A) NAME/KEY:
- (B) LOCATION:
- (D) OTHER INFORMATION: 11BR primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:39:

20

CATTAAAGC ACATACATCT TG

22

(2) INFORMATION FOR SEQ ID NO:40:

25

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 21 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

30

- (A) NAME/KEY:
- (B) LOCATION:
- (D) OTHER INFORMATION: 11CF primer

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:40:

TCTAGAGGCA AAGAATCATA C

21

40

(2) INFORMATION FOR SEQ ID NO:41:

(i) SEQUENCE CHARACTERISTICS:

45

- (A) LENGTH: 22 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

50

- (A) NAME/KEY:
- (B) LOCATION:
- (D) OTHER INFORMATION: 11CR primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:41:

55

CAAGATTATT CCTTTCATTA GC

22

(2) INFORMATION FOR SEQ ID NO:42:

(i) SEQUENCE CHARACTERISTICS:

60

- (A) LENGTH: 22 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single

(D) TOPOLOGY: linear

- 5 (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 11DF primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:42:

10 AACCAAAACA CAAATCTAAG AG 22

(2) INFORMATION FOR SEQ ID NO:43:

- 15 (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 23 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

20

- (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 11DR primer

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:43:

GTCATTTTTA TATGCTGCTT TAC 23

30 (2) INFORMATION FOR SEQ ID NO:44:

- (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 21 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

35

- (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 11EF primer

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:44:

45 GGTTTTATAT GGAGACACAG G 21

(2) INFORMATION FOR SEQ ID NO:45:

- 50 (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 23 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

55

- (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 11ER primer

60 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:45:

GTATTACAA TTTCAACACA AGC 23



## (2) INFORMATION FOR SEQ ID NO:46:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(A) NAME/KEY:

(B) LOCATION:

(D) OTHER INFORMATION: 11FF primer

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:46:

ATCACAGTTT TGGAGGTAGC

20

## (2) INFORMATION FOR SEQ ID NO:47:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 21 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(A) NAME/KEY:

(B) LOCATION:

(D) OTHER INFORMATION: 11FR primer

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:47:

CTGACTTCCT GATTCTTCTA A

21

## (2) INFORMATION FOR SEQ ID NO:48:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 21 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(A) NAME/KEY:

(B) LOCATION:

(D) OTHER INFORMATION: 11GF primer

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:48:

CTCAGATGTT ATTTCCAAG C .

21

## (2) INFORMATION FOR SEQ ID NO:49:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 21 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 11GR primer

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:49:  
CTGTTAAATA ACCAGAAGCA C 21

10 (2) INFORMATION FOR SEQ ID NO:50:  
(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 18 base pairs  
(B) TYPE: nucleic acid  
15 (C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(A) NAME/KEY:  
20 (B) LOCATION:  
(D) OTHER INFORMATION: 11HF primer  
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:50:  
25 AGGTAGACAG CAGCAAGC 18

(2) INFORMATION FOR SEQ ID NO:51:  
(i) SEQUENCE CHARACTERISTICS:  
30 (A) LENGTH: 22 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

35 (ix) FEATURE:  
(A) NAME/KEY: None  
(B) LOCATION:  
(D) OTHER INFORMATION: 11HR primer  
40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:51:  
GTAATATCAG TTGGCATTTA TT 22

45 (2) INFORMATION FOR SEQ ID NO:52:  
(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 21 base pairs  
(B) TYPE: nucleic acid  
50 (C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(A) NAME/KEY:  
55 (B) LOCATION:  
(D) OTHER INFORMATION: 11IF primer  
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:52:  
60 TGCAGAGGTA CATCCAATAA G 21

(2) INFORMATION FOR SEQ ID NO:53:

(i) SEQUENCE CHARACTERISTICS:  
5 (A) LENGTH: 21 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

10 (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 11IR primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:53:  
15 GATCAGTAAA TAGCAAGTCC G 21

(2) INFORMATION FOR SEQ ID NO:54:

20 (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 23 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
25 (D) TOPOLOGY: linear

(A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 11JF primer  
30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:54:  
TACTGAAAAT GAAGATAACA AAT 23

(2) INFORMATION FOR SEQ ID NO:55:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 22 base pairs  
(B) TYPE: nucleic acid  
40 (C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(A) NAME/KEY:  
45 (B) LOCATION:  
(D) OTHER INFORMATION: !!JR primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:55:  
50 ATTTTGGTCT TTCTTATGTC AG 22

(2) INFORMATION FOR SEQ ID NO:56:

(i) SEQUENCE CHARACTERISTICS:  
55 (A) LENGTH: 35 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

60 (A) NAME/KEY:  
(B) LOCATION:

(D) OTHER INFORMATION: 11KF-M13 primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:56:

5

TGTAAACGA CGGCCAGTCT ACTAAACGG AGCAA

35

(2) INFORMATION FOR SEQ ID NO:57:

10

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 35 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

15

(A) NAME/KEY:

(B) LOCATION:

(D) OTHER INFORMATION: 11KR-M13 primer

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:57:

CAGGAAACAG CTATGACCGT ATGAAAACCC AACAG

35

25

(2) INFORMATION FOR SEQ ID NO:58:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 22 base pairs

(B) TYPE: nucleic acid

30

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(A) NAME/KEY:

35

(B) LOCATION:

(D) OTHER INFORMATION: 11LF primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:58:

40

CACAAAATAC TGAAAGAAAG TG

22

(2) INFORMATION FOR SEQ ID NO:59:

(i) SEQUENCE CHARACTERISTICS:

45

(A) LENGTH: 19 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

50

(A) NAME/KEY:

(B) LOCATION:

(D) OTHER INFORMATION: 11LR primer

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:59:

GGCACACAG TCTCAATAG

19

(2) INFORMATION FOR SEQ ID NO:60:

60

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 20 base pairs

(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

5

(A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 11MF primer

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:60:

GCAAAGACCC TAAAGTACAG 20

15

(2) INFORMATION FOR SEQ ID NO:61:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 22 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

20

(A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 11MR primer

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:61:

30 CATCAAATAT TCCTTCTCTA AG 22

(2) INFORMATION FOR SEQ ID NO:62:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 35 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

35

(A) NAME, KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 11NF-M13 primer

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:62:

45 TGTAACACGA CGGCCAGTGA AAATTCAGCC TTAGC 35

(2) INFORMATION FOR SEQ ID NO:63:

50

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 35 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

55

(A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 11NR-M13 primer

60

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:63:

CAGGAAACAG CTATGACCAT CAGAAATGGTA GGAAT

35

5 (2) INFORMATION FOR SEQ ID NO:64:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 22 base pairs
- (B) TYPE: nucleic acid
- 10 (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

- (A) NAME/KEY:
- 15 (B) LOCATION:
- (D) OTHER INFORMATION: 110F primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:64:

20 GTACTATAGC TGAAAATGAC AA

22

(2) INFORMATION FOR SEQ ID NO:65:

(i) SEQUENCE CHARACTERISTICS:

- 25 (A) LENGTH: 20 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

- 30 (A) NAME/KEY:
- (B) LOCATION:
- (D) OTHER INFORMATION: 110R primer

35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:65:

ACCACTGGCT ATCCTAAATG

20

(2) INFORMATION FOR SEQ ID NO:66:

40 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- 45 (D) TOPOLOGY: linear

- (A) NAME/KEY:
- (B) LOCATION:
- 50 (D) OTHER INFORMATION: 11PF primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:66:

TGAAGATATT TCGTTGAGG

20

55 (2) INFORMATION FOR SEQ ID NO:67:

(i) SEQUENCE CHARACTERISTICS:

- 60 (A) LENGTH: 20 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

5 (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 11PR primer  
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:67:

10 GTCAGCAAAA ACCTTATGTG 20  
(2) INFORMATION FOR SEQ ID NO:68:

15 (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 21 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

20 (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 11QF primer  
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:68:

25 ACGAAAATTA TGGCAGGTTG T 21  
(2) INFORMATION FOR SEQ ID NO:69:

30 (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 21 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

35 (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 11QR primer  
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:69:

40 CTTGTCTTGC GTTTTGTAAT G 21  
(2) INFORMATION FOR SEQ ID NO:70:

45 (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

50 (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 11RF primer  
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:70:

55 GCTTCATAAG TCAGTCTCAT 20

## (2) INFORMATION FOR SEQ ID NO:71:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(A) NAME/KEY:

(B) LOCATION:

(D) OTHER INFORMATION: 11RR primer

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:71:

TCAAATTCCT CTAACACTCC

20

## (2) INFORMATION FOR SEQ ID NO:72:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 35 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(A) NAME/KEY:

(B) LOCATION:

(D) OTHER INFORMATION: 11SF-M13 primer

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:72:

TGTAACACGA CGGCCAGTTA CAGCAAGTGG AAAGC

35

## (2) INFORMATION FOR SEQ ID NO:73:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 37 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(A) NAME/KEY:

(B) LOCATION:

(D) OTHER INFORMATION: 11SR-M13 primer

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:73:

CAGGAAACAG CTATGACCAA GTTTCAGTTT TACCAAT

37

## (2) INFORMATION FOR SEQ ID NO:74:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 22 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(A) NAME/KEY:



- (B) LOCATION:
- (D) OTHER INFORMATION: 11TF primer

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:74:

GTTCTTCAGA AAATAATCAC TC

22

(2) INFORMATION FOR SEQ ID NO:75:

10

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 21 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

15

(A) NAME/KEY:

(B) LOCATION:

20

(D) OTHER INFORMATION: 11TR primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:75:

TGTAAAAGA GAATGTGTGG C

21

25

(2) INFORMATION FOR SEQ ID NO:76:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 39 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

30

35

(A) NAME/KEY:

(B) LOCATION:

(D) OTHER INFORMATION: 11UF-M13 primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:76:

40

TGTAAAACGA CGGCCAGTAC TTTTCTGAT GTTCCTGTG

39

(2) INFORMATION FOR SEQ ID NO:77:

45

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 39 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

50

(A) NAME/KEY:

(B) LOCATION:

(D) OTHER INFORMATION: 11UR-M13 primer

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:77:

CAGGAAACAG CTATGACCTA AAAATAGTGA TTGGCAACA

39

60

(2) INFORMATION FOR SEQ ID NO:78:

(i) SEQUENCE CHARACTERISTICS:

5 (A) LENGTH: 42 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

10 (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 12F/M13F primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:78:  
15 TGTA AACGA CGGCCAGTAG TGGTGT TTA AAGTGGTCAA AA 42

(2) INFORMATION FOR SEQ ID NO:79:

(i) SEQUENCE CHARACTERISTICS:  
20 (A) LENGTH: 40 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

25 (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 12R/M13R primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:79:  
30 CAGGAAACAG CTATGACCGG ATCCACCTGA GGTCAGAATA 40

(2) INFORMATION FOR SEQ ID NO:80:

35 (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 21 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
40 (D) TOPOLOGY: linear

(A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 13-2F primer

45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:80:  
TAACATTTAA GCATCCGTTA C 21

50 (2) INFORMATION FOR SEQ ID NO:81:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 28 base pairs  
55 (B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

60 (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 13-2R primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:81:

AAACGAGACT TTTCTCATAC TGTATTAG

28

5

(2) INFORMATION FOR SEQ ID NO:82:

(i) SEQUENCE CHARACTERISTICS:

- 10 (A) LENGTH: 22 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

15

- (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 14F primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:82:

20

ACCATGTAGC AAATGAGGGT CT

22

(2) INFORMATION FOR SEQ ID NO:83:

25

(i) SEQUENCE CHARACTERISTICS:

- 30 (A) LENGTH: 22 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

30

- (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 14AR primer

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:83:

GCTTTTGTCT GTTTCCTCC AA

22

40

(2) INFORMATION FOR SEQ ID NO:84:

(i) SEQUENCE CHARACTERISTICS:

- 45 (A) LENGTH: 21 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

45

- (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 15-2F primer

50

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:84:

CCAGGGGTG TGCTTTTAA A

21

55

(2) INFORMATION FOR SEQ ID NO:85:

(i) SEQUENCE CHARACTERISTICS:

- 60 (A) LENGTH: 38 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single

60

(D) TOPOLOGY: linear

- 5 (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 15FUT/M13-R primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:85:

10 CAGGAAACAG CTATGACCAC TCTGTCATAA AAGCCATC 38

(2) INFORMATION FOR SEQ ID NO:86:

- 15 (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 24 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

20

- (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 16AF primer

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:86:

TTTGTTTGT TATAATTGTT TTTA 24

30 (2) INFORMATION FOR SEQ ID NO:87:

- (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

35

- (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 16AR primer

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:87:

45 CCAACTTTTT AGTTCGAGAG 20

(2) INFORMATION FOR SEQ ID NO:88:

- (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 19 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

50

55

- (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 17F primer

60

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:88:

TTCAGTATCA TCCTATGTG 19

## (2) INFORMATION FOR SEQ ID NO:89:

## 5 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

10

- (A) NAME/KEY:
- (B) LOCATION:
- (D) OTHER INFORMATION: 17AR primer

15

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:89:

AGAAACCTTA ACCCATACTG

20

20

## (2) INFORMATION FOR SEQ ID NO:90:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 39 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

25

- (A) NAME/KEY:
- (B) LOCATION:
- (D) OTHER INFORMATION: 18FUT/M13-AF primer

30

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:90:

35 TGTAACACGA CGGCCAGTGA ATTCTAGAGT CACACTTCC

39

## (2) INFORMATION FOR SEQ ID NO:91:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 38 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

40

- (A) NAME/KEY:
- (B) LOCATION:
- (D) OTHER INFORMATION: 18R/M13R primer

45

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:91:

50

CAGGAAACAG CTATGACCTT TAACTGAATC AATGACTG

38

## (2) INFORMATION FOR SEQ ID NO:92:

55

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 41 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

60

(A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 19F/M13F primer

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:92:  
TGTAACACGA CGGCCAGTAA GTGAATATTT TTAAGGCAGT T 41

10 (2) INFORMATION FOR SEQ ID NO:93:  
(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 39 base pairs  
(B) TYPE: nucleic acid  
15 (C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(A) NAME/KEY:  
20 (B) LOCATION:  
(D) OTHER INFORMATION: 19FUT/M13-R primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:93:  
25 CAGGAAACAG CTATGACCAA GAGACCGAAA CTCCATCTC 39

(2) INFORMATION FOR SEQ ID NO:94:  
(i) SEQUENCE CHARACTERISTICS:  
30 (A) LENGTH: 38 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

35 (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 20F/M13F primer

40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:94:  
TGTAACACGA CGGCCAGTCA CTGTGCCTGG CCTGATAC 38

(2) INFORMATION FOR SEQ ID NO:95:  
45 (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 39 base pairs  
(B) TYPE: nucleic acid  
50 (C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(A) NAME/KEY:  
(B) LOCATION:  
55 (D) OTHER INFORMATION: 20R/M13R primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:95:  
60 CAGGAAACAG CTATGACCAT GTTAAATTCA AAGTCTCTA 39

(2) INFORMATION FOR SEQ ID NO:96:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 39 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 21F/M13F primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:96:

TGTAAACGA CGGCCAGTGG GTGTTTTATG CTTGGTTCT

(2) INFORMATION FOR SEQ ID NO:97:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 40 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 21R/M13R primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:97:

CAGGAAACAG CTATGACCCA TTTCAACATA TTCCTTCCTG

(2) INFORMATION FOR SEQ ID NO:98:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 19 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 22F-1A primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:98:

AACCACACCC TTAAGATGA

(2) INFORMATION FOR SEQ ID NO:99:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 22R-1A primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:99:

5 GCATTAGTAG TGGATTTTGC 20

(2) INFORMATION FOR SEQ ID NO:100:

(i) SEQUENCE CHARACTERISTICS:

10 (A) LENGTH: 16 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

15 (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 23FII primer

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:100:

TCACTTCCAT TGCATC 16

(2) INFORMATION FOR SEQ ID NO:101:

25 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 17 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
30 (D) TOPOLOGY: linear

(A) NAME/KEY:  
(B) LOCATION:  
35 (D) OTHER INFORMATION: 23RII primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:101:

40 TGCCAACTGG TAGCTCC 17

(2) INFORMATION FOR SEQ ID NO:102:

(i) SEQUENCE CHARACTERISTICS:

45 (A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

50 (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 24 2F primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:102:

55 TACAGTTAGC AGCGACAAAA 20

(2) INFORMATION FOR SEQ ID NO:103:

60 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 38 base pairs  
(B) TYPE: nucleic acid



(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

5

(A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 24R/M13R primer

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:103:

CAGGAAACAG CTATGACCAT TTGCCAACTG GTAGCTCC

38

(2) INFORMATION FOR SEQ ID NO:104:

15

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

20

(A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 25F-7/23 primer

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:104:

GCTTTCGCCA AATTCAGCTA

20

30

(2) INFORMATION FOR SEQ ID NO:105:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

35

(A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 25R-7/23 primer

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:105:

45

TACCAAAATG TGTGGTGATG

20

(2) INFORMATION FOR SEQ ID NO:106:

50

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

55

(A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 26-2F primer

60

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:106:

AATCACTGAT ACTGGTTTTG

20

(2) INFORMATION FOR SEQ ID NO:107:

5

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 20 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

10

(D) TOPOLOGY: linear

(A) NAME/KEY:

(B) LOCATION:

15

(D) OTHER INFORMATION: 26-2R primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:107:

TATACTTACA GGAGCCACAT

20

20

(2) INFORMATION FOR SEQ ID NO:108:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 18 base pairs

25

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(A) NAME/KEY:

(B) LOCATION:

30

(D) OTHER INFORMATION: 27AF-1A primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:108:

35

CTGTGTGTAA TATTTGCG

18

(2) INFORMATION FOR SEQ ID NO:109:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 40 base pairs

40

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

45

(A) NAME/KEY:

(B) LOCATION:

(D) OTHER INFORMATION: 27AR/M13R primer

50

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:109:

CAGGAAACAG CTATGACGGC AAGTTCTTCG TCAGCTATTG

40

55

(2) INFORMATION FOR SEQ ID NO:110:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 40 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

60

(D) TOPOLOGY: linear

5 (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 27BF/M13F primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:110:  
TGTAACACGA CGGCCAGTGA ATTCTCCTCA GATGACTCCA 40

10 (2) INFORMATION FOR SEQ ID NO:111:

(i) SEQUENCE CHARACTERISTICS:  
15 (A) LENGTH: 38 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

20 (A) NAME/KEY:  
(B) LOCATION:  
(D) OTHER INFORMATION: 27BR/M13R primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:111:  
25 CAGGAAACAG CTATGACCTC TTTGCTCATT GTGCAACA 38

**WE CLAIM:**

- 5 1. A genomic DNA containing a BRCA2 gene,  
wherein the first twelve nucleotides beginning exon 5 are 5'-  
TCCTGTTGTTCT-3' as set forth in SEQ. ID. NO: 1,  
wherein nucleotides numbers 5782-5790 are GTTTGTGTT as set forth in  
SEQ. ID. NO: 4, and  
10 wherein the last 20 nucleotides ending exon 15 are 5'-  
CTGCGTGTTCATACAAACAG-3' as set forth in SEQ. ID. NO: 2 and the first 20  
nucleotides beginning exon 16 are 5'-CTGTATACGTATGGCGTTTC-3' as set forth  
in SEQ. ID. NO: 3.

- 15 2. The genomic DNA according to claim 1 wherein the coding sequence  
nucleotides are as follows:

20 1093 A  
1342 A  
1593 A  
2457 T  
2908 G  
3199 A  
3624 A  
4035 T  
25 7470 A  
9079 G.

3. The genomic DNA according to claim 1 wherein the coding sequence  
nucleotides are as follows:

30 1093 A  
1342 C  
1593 A  
2457 T  
35 2908 G  
3199 A  
3624 A  
4035 T  
7470 A  
40 9079 G.

4. The genomic DNA according to claim 1 wherein the coding sequence  
nucleotides are as follows:

5           1093 A  
            1342 C  
            1593 A  
            2457 T  
            2908 G  
            3199 A  
            3624 A  
10           4035 C  
            7470 A  
            9079 G.

15       5.     The genomic DNA according to claim 1 wherein the coding sequence  
nucleotides are as follows:

20           1093 C  
            1342 A  
            1593 A  
            2457 C  
            2908 G  
            3199 G  
            3624 G  
25           4035 T  
            7470 G  
            9079 G.

30       6.     The genomic DNA according to claim 1 wherein the coding sequence  
nucleotides are as follows:

35           1093 A  
            1342 C  
            1593 A  
            2457 T  
            2908 G  
            3199 A  
            3624 G  
40           4035 T  
            7470 G  
            9079 G.

45       7.     The genomic DNA according to claim 1 wherein the coding sequence  
nucleotides are as follows:

50           1093 C  
            1342 C  
            1593 G  
            2457 C  
            2908 A  
            3199 G

5           3624 A  
            4035 T  
            7470 A  
            9079 A.

8.     The genomic DNA according to claim 1 wherein the coding sequence nucleotides are as follows:

10           2024 C  
            4553 C  
            4815 G  
            5841 T  
            5972 C.

15     9.     A DNA comprising a BRCA2 coding sequence,  
            wherein nucleotide numbers 643-666 are  
CTTAGTGAAAGTCCTGTTGTTCTA and  
            wherein nucleotides numbers 5782-5790 are GTTTGTGTT.

20     10.    The DNA according to claim 9 wherein the coding sequence nucleotides are  
as follows:

25           1093 A  
            1342 A  
            1593 A  
            2457 T  
            2908 G  
            3199 A  
30           3624 A  
            4035 T  
            7470 A  
            9079 G.

35     11.    The DNA according to claim 9 wherein the coding sequence nucleotides are  
as follows:

40           1093 A  
            1342 C  
            1593 A  
            2457 T  
            2908 G  
            3199 A  
            3624 A  
45           4035 T  
            7470 A  
            9079 G

as set forth in SEQ. ID. NO: 4.

50     12.    The DNA according to claim 9 wherein the coding sequence nucleotides are  
as follows:

5           1093 A  
            1342 C  
            1593 A  
            2457 T  
            2908 G  
            3199 A  
            3624 A  
10           4035 C  
            7470 A  
            9079 G

as set forth in SEQ. ID. NO: 6.

15   13.   The DNA according to claim 9 wherein the coding sequence nucleotides are as follows:

20           1093 C  
            1342 A  
            1593 A  
            2457 C  
            2908 G  
            3199 G  
            3624 G  
25           4035 T  
            7470 G  
            9079 G

as set forth in SEQ. ID. NO: 8.

30   14.   The DNA according to claim 9 wherein the coding sequence nucleotides are as follows:

35           1093 A  
            1342 C  
            1593 A  
            2457 T  
            2908 G  
            3199 A  
            3624 G  
40           4035 T  
            7470 G  
            9079 G

as set forth in SEQ. ID. NO: 10.

45   15.   The DNA according to claim 9 wherein the coding sequence nucleotides are as follows:

50           1093 C  
            1342 C  
            1593 G  
            2457 C

2908 A  
3199 G  
3624 A  
5 4035 T  
7470 A  
9079 A

as set forth in SEQ. ID. NO: 12.

10 16. The DNA according to claim 9 wherein the coding sequence nucleotides are as follows:

2024 C  
4553 C  
15 4815 G  
5841 T  
5972 C.

20 17. A BRCA2 protein having the following amino acids at the following peptide numbers:

289 asparagine  
372 histidine  
894 valine  
25 991 asparagine  
1852 valine  
1853 cysteine  
1854 valine  
2951 alanine

30 as set forth in SEQ. ID. NO: 5.

18. The BRCA2 protein having the following amino acids at the following peptide numbers:

35 289 asparagine  
372 asparagine  
599 serine  
894 valine  
991 asparagine  
40 2951 alanine.

19. The BRCA2 protein having the following amino acids at the following peptide numbers:

45 289 histidine  
372 histidine  
894 valine  
991 asparatic acid  
2951 alanine

50 as set forth in SEQ. ID. NO: 9.



20. The BRCA2 protein having the following amino acids at the following peptide numbers:

- 5            289    histidine  
             372    asparagine  
             894    isoleucine  
             991    aspartic acid  
             2951   threonine  
10   as set forth in SEQ. ID. NO: 13.

21. The BRCA2 protein according to claims 17-20 having the following amino acids at the following peptide numbers:

- 15           590    serine  
             1442   serine  
             1915   threonine.

22. A haplotype of BRCA2 coding sequence (BRCA2<sup>omi 1</sup>) as set forth in SEQ. ID.  
20   NO: 4 or a sequence complementary thereto.

23. A BRCA2 protein comprising an amino acid sequence derived from BRCA2<sup>omi 1</sup> as set forth in SEQ. ID. NO: 5.

- 25   24. A haplotype of BRCA2 coding sequence (BRCA2<sup>omi 2</sup>) as set forth in SEQ. ID.  
NO: 6 or a sequence complementary thereto.

25. A BRCA2 protein comprising an amino acid sequence derived from BRCA2<sup>omi 2</sup> as set forth in SEQ. ID. NO: 7.

30

26. A haplotype of BRCA2 coding sequence (BRCA2<sup>omi 3</sup>) as set forth in SEQ. ID.  
NO: 8 or a sequence complementary thereto.

27. A BRCA2 protein comprising an amino acid sequence derived from BRCA2<sup>omi 3</sup> as set forth in SEQ. ID. NO: 9.  
35

28. A haplotype of BRCA2 coding sequence (BRCA2<sup>omi 4</sup>) as set forth in SEQ. ID. NO: 10 or a sequence complementary thereto.

5 29. A BRCA2 protein comprising an amino acid sequence derived from BRCA2<sup>omi 4</sup> as set forth in SEQ. ID. NO: 11.

30. A haplotype of BRCA2 coding sequence (BRCA2<sup>omi 5</sup>) as set forth in SEQ. ID. NO: 12 or a sequence complementary thereto.

10

31. A BRCA2 protein comprising an amino acid sequence derived from BRCA2<sup>omi 5</sup> as set forth in SEQ. ID. NO: 13.

15 32. A method of identifying individuals having a BRCA2 gene with a BRCA2 coding sequence not associated with disease, comprising:

- (a) amplifying a DNA or a fragment thereof of an individual's BRCA2 coding sequence;
- (b) sequencing said amplified DNA fragment;
- (c) if necessary, repeating steps (a) and (b) until said individual's BRCA2 coding sequence is sufficiently sequenced to determine whether a mutation is present;
- (d) comparing the sequence of said amplified DNA fragment to a BRCA2<sup>(omi)</sup> DNA sequence selecting from the group consisting of SEQ. ID. NO: 4, SEQ. ID. NO: 6, SEQ. ID. NO: 8, SEQ. ID. NO: 10, SEQ. ID. NO: 12, and their respective complementary sequences;
- (e) determining the presence of absence of each of the following polymorphic variations in said individual's BRCA2 coding sequence:
  - (i) AAT and CAT at position 1093,
  - (ii) CAT and AAT at position 1342,
  - (iii) TCA and TCG at position 1593,

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- (iv) CAT and CAC at position 2457,  
(v) GTA and ATA at position 2908,  
(vi) AAC and GAC at position 3199,  
5 (vii) AAA and AAG at position 3624,  
(viii) GTT and GTC at position 4035,  
(ix) TCA and TCG at position 7470, and  
(x) GCC and ACC at position 9079; and
- (f) determining any sequence differences between said individual's  
10 BRCA2 coding sequences and a BRCA2<sup>(omi)</sup> DNA sequence selected  
from the group consisting of SEQ. ID. NO: 4, SEQ. ID. NO: 6, SEQ. ID.  
NO: 8, SEQ. ID. NO: 10, SEQ. ID. NO: 12, and their respective  
complementary sequences, wherein the presence of said polymorphic  
variations and the absence of a variation outside of positions 1093,  
15 1342, 1593, 2457, 2908, 3199, 3624, 4035, 7470, and 9079 is  
correlated with an absence of increased genetic susceptibility to breast  
or ovarian cancer resulting from a BRCA2 mutation in the BRCA2  
coding sequence.
33. A method of identifying individuals having a BRCA2 gene with a BRCA2  
20 coding sequence not associated with disease, comprising:
- (a) amplifying a DNA or a fragment thereof of an individual's BRCA2  
coding sequence;
- (b) sequencing said amplified DNA fragment;
- (c) if necessary, repeating steps (a) and (b) until said individual's BRCA2  
25 coding sequence is sufficiently sequenced to determine whether a  
mutation is present;
- (d) comparing the sequence of said amplified DNA fragment to a  
BRCA2<sup>(omi)</sup> DNA sequence selecting from the group consisting of SEQ.  
ID. NO: 4, SEQ. ID. NO: 6, SEQ. ID. NO: 8, SEQ. ID. NO: 10, SEQ. ID.  
30 NO: 12, and their respective complementary sequences;

(e) determining the presence of absence of each of the following polymorphic variations in said individual's BRCA2 coding sequence:

- (i) AAT and CAT at position 1093,
- (ii) CAT and AAT at position 1342,
- (iii) TCA and TCG at position 1593,
- (iv) CAT and CAC at position 2457,
- (v) GTA and ATA at position 2908,
- (vi) AAC and GAC at position 3199,
- (vii) AAA and AAG at position 3624,
- (viii) GTT and GTC at position 4035,
- (ix) TCA and TCG at position 7470, and
- (x) GCC and ACC at position 9079; and

(f) determining any sequence differences between said individual's BRCA2 coding sequences and a BRCA2<sup>(oml)</sup> DNA sequence selected from the group consisting of SEQ. ID. NO: 4, SEQ. ID. NO: 6, SEQ. ID. NO: 8, SEQ. ID. NO: 10, SEQ. ID. NO: 12, and their respective complementary sequences, wherein the presence of said polymorphic variations and the absence of a variation outside of positions 1093, 1342, 1593, 2457, 2908, 3199, 3624, 4035, 7470, and 9079 is correlated with an absence of increased genetic susceptibility to breast or ovarian cancer resulting from a BRCA2 mutation in the BRCA2 coding sequence; wherein, codon variations occur at the following frequencies, respectively, in a Caucasian population of individuals free of disease:

- (i) at position 1093, AAT and CAT occur at frequencies from about 75-85%, and from about 15-25%, respectively,
- (ii) at position 1342, CAT and AAT occur at frequencies from about 35-45%, and from about 55-65%, respectively,
- (iii) at position 1593, TCA and TCG occur at frequencies from about 85-95%, and from about 5-15%, respectively,

- 5 (iv) at position 2457, CAT and CAC occur at frequencies from about 75-85%, and from about 15-25%, respectively,
- (v) at position 2908, GTA and ATA occur at frequencies from about 85-95%, and from about 5-15%, respectively,
- (vi) at position 3199, AAC and GAC occur at frequencies from about 75-85%, and from about 15-25%, respectively,
- 10 (vii) at position 3674, AAA and AAG occur at frequencies from about 75-85%, and from about 15-25%, respectively,
- (viii) at position 4035, GTT and GTC occur at frequencies from about 85-95%, and from about 5-15%, respectively,
- (ix) at position 7470, TCA and TCG occur at frequencies from about 75-85%, and from about 15-25%, respectively, and
- 15 (x) at position 9079, GCC and ACC occur at frequencies from about 85-95%, and from about 5-15%, respectively.

34. A method of detecting an increased genetic susceptibility to breast and ovarian cancer in an individual resulting from the presence of a mutation in the BRCA2 coding sequence, comprising:

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- (a) amplifying a DNA or a fragment thereof of an individual's BRCA2 coding sequence;
- (b) sequencing said amplified DNA fragment;
- 25 (c) if necessary, repeating steps (a) and (b) until said individual's BRCA2 coding sequence is sufficiently sequenced to determine whether a mutation is present;
- (d) comparing the sequence of said amplified DNA fragment to a BRCA2<sup>(omi)</sup> DNA sequence selected from the group consisting of SEQ.

ID. NO: 4, SEQ. ID. NO: 6, SEQ. ID. NO: 8, SEQ. ID. NO: 10, SEQ. ID. NO: 12, and their respective complementary sequences;

- (e) determining any sequence differences between said individual's  
5 BRCA2 coding sequences and a BRCA2<sup>(omi)</sup> DNA sequence selected  
from the group consisting of SEQ. ID. NO: 4, SEQ. ID. NO: 6, SEQ. ID.  
NO: 8, SEQ. ID. NO: 10, SEQ. ID. NO: 12, and their respective  
complementary sequences in order to determine the presence or  
absence of base changes in said individual's BRCA2 coding sequence  
10 wherein a base change which is not any one of the following:

- (i) AAT and CAT at position 1093,
- (ii) CAT and AAT at position 1342,
- (iii) TCA and TCG at position 1593,
- (iv) CAT and CAC at position 2457,
- 15 (v) GTA and ATA at position 2908,
- (vi) AAC and GAC at position 3199,
- (vii) AAA and AAG at position 3624,
- (viii) GTT and GTC at position 4035,
- (ix) TCA and TCG at position 7470, and
- 20 (x) GCC and ACC at position 9079, is correlated with the

potential of increased genetic susceptibility to breast or ovarian cancer  
resulting from a BRCA2 mutation in the BRCA2 coding sequence.

35. A method of detecting an increased genetic susceptibility to breast and  
ovarian cancer in an individual resulting from the presence of a mutation in the  
25 BRCA2 coding sequence, comprising:

- (a) amplifying a DNA or a fragment thereof of an individual's BRCA2  
coding sequence;
- (b) sequencing said amplified DNA fragment;

- (c) if necessary, repeating steps (a) and (b) until said individual's BRCA2 coding sequence is sufficiently sequenced to determine whether a mutation is present;
- 5 (d) comparing the sequence of said amplified DNA fragment to a BRCA2<sup>(omi)</sup> DNA sequence selected from the group consisting of: SEQ. ID. NO: 4, SEQ. ID. NO: 6, SEQ. ID. NO: 8, SEQ. ID. NO: 10, SEQ. ID. NO: 12, and their respective complementary sequences;
- 10 (e) determining any sequence differences between said individual's BRCA2 coding sequences and a BRCA2<sup>(omi)</sup> DNA sequence selected from the group consisting of: SEQ. ID. NO: 4, SEQ. ID. NO: 6, SEQ. ID. NO: 8, SEQ. ID. NO: 10, SEQ. ID. NO: 12, and their respective complementary sequences in order to determine the presence or absence of base changes in said individual's BRCA2 coding sequence
- 15 wherein a base change which is not any one of the following:
- (i) AAT and CAT at position 1093,
  - (ii) CAT and AAT at position 1342,
  - (iii) TCA and TCG at position 1593,
  - (iv) CAT and CAC at position 2457,
  - 20 (v) GTA and ATA at position 2908,
  - (vi) AAC and GAC at position 3199,
  - (vii) AAA and AAG at position 3624,
  - (viii) GTT and GTC at position 4035,
  - (ix) TCA and TCG at position 7470, and
  - 25 (x) GCC and ACC at position 9079, is correlated with the potential of increased genetic susceptibility to breast or ovarian cancer resulting from a BRCA2 mutation in the BRCA2 coding sequence, wherein, codon variations occur at the following frequencies, respectively, in a Caucasian population of individuals free of disease:

- 5 (i) at position 1093, AAT and CAT occur at frequencies from about 75-85%, and from about 15-25%, respectively,
- (ii) at position 1342, CAT and AAT occur at frequencies from about 35-45%, and from about 55-65%, respectively,
- (iii) at position 1593, TCA and TCG occur at frequencies from about 85-95%, and from about 5-15%, respectively,
- (iv) at position 2457, CAT and CAC occur at frequencies from about 75-85%, and from about 15-25%, respectively,
- 10 (v) at position 2908, GTA and ATA occur at frequencies from about 85-95%, and from about 5-15%, respectively,
- (vi) at position 3199, AAC and GAC occur at frequencies from about 75-85%, and from about 15-25%, respectively,
- 15 (vii) at position 3624, AAA and AAG occur at frequencies from about 75-85%, and from about 15-25%, respectively,
- (viii) at position 4035, GTT and GTC occur at frequencies from about 85-95%, and from about 5-15%, respectively,
- 20 (ix) at position 7470, TCA and TCG occur at frequencies from about 75-85%, and from about 15-25%, respectively, and
- (x) at position 9079, GCC and ACC occur at frequencies from about 85-95%, and from about 5-15%, respectively.

25 36. A method according to any of the claims 32-35 wherein the said amplifying is performed by annealing at least one oligonucleotide primer to said DNA fragment and extending the oligonucleotide primer by an agent for polymerization.



37. A method according to claim 36 wherein said oligonucleotide primer is directly or indirectly labeled with a radioactive label, a fluorescent label, a bioluminescent label, a chemiluminescent label, a metal chelator, or an enzyme label.

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38. A BRCA2 coding sequence according to claims 32, wherein the codon pairs occur at the following frequencies:

- (i) at position 1093, AAT and CAT occur at frequencies from about 75-85%, and from about 15-25%, respectively,
- 10 (ii) at position 1342, CAT and AAT occur at frequencies from about 35-45%, and from about 55-65%, respectively,
- (iii) at position 1593, TCA and TCG occur at frequencies from about 85-95%, and from about 5-15%, respectively,
- (iv) at position 2457, CAT and CAC occur at frequencies from about 75-85%, and from about 15-25%, respectively,
- 15 (v) at position 2908, GTA and ATA occur at frequencies from about 85-95%, and from about 5-15%, respectively,
- (vi) at position 3199, AAC and GAC occur at frequencies from about 75-85%, and from about 15-25%,  
20 respectively,
- (vii) at position 3624, AAA and AAG occur at frequencies from about 75-85%, and from about 15-25%,  
respectively,
- (viii) at position 4035, GTT and GTC occur at frequencies from about 85-95%, and from about 5-15%, respectively,
- 25 (ix) at position 7470, TCA and TCG occur at frequencies from about 75-85%, and from about 15-25%, respectively, and
- (x) at position 9079, GCC and ACC occur at frequencies from about 85-95%, and from about 5-15%, respectively.

30

39. An oligonucleotide primer capable of hybridizing to a sample of BRCA2 gene, or its respective complementary sequences selected from the group consisting of SEQ. ID. NO: 14, 19, 22, 23, 25, 26, 29-76, 83, 85-88, 90, 91, 97, 98, 101, and 104-  
5 107.

40. A chip array having "n" elements for performing allele specific sequence-based techniques comprising a solid phase chip and oligonucleotides having "n" different nucleotide sequences,

10 wherein "n" is an interger greater than or equal to ten,  
wherein said oligonucleotides are bound to said solid phase chip in a manner which permits said oligonucleotides to effectively hybridize to complementary oligonucleotides or polynucleotides,

15 wherein oligonucleotides having different nucleotide sequence are bound to said solid phase chip at different locations so that a particular location on said solid phase chip exclusively binds oligonucleotides having a specific nucleotide sequence, and

20 wherein at least ten oligonucleotides are capable of specifically hybridizing to the BRCA2 DNA having the sequence as set forth in SEQ. ID. NO: 4, SEQ. ID. NO: 6, SEQ. ID. NO: 8, SEQ. ID. NO: 10, SEQ. ID. NO: 12 or their respective complementary sequences, at least one oligonucleotide being capable of specifically hybridizing at each of the nucleotide positions 1093, 1342, 1593, 2457, 2908, 3199, 3624, 4035, 7470, 9079, or complementary thereto.

25 41. A method of performing gene therapy on a patient, comprising:

a) contacting cancer cells *in vivo* with an effective amount of a vector comprising DNA containing at least a portion of BRCA2 sequence selected from the group consisting of SEQ. ID. NO: 4, SEQ. ID. NO: 6, SEQ. ID. NO: 8, SEQ. ID. NO: 10, SEQ. ID. NO: 12, or their respective complementary sequences

30 b) allowing the vector to enter the cancer cells, and  
c) measuring a reduction in tumor growth.

42. The method according to claim 41 wherein said cancer cells have a mutation in the BRCA2 gene.

43. The method according to claim 41 wherein said patient has a mutation in the BRCA2 gene of non-cancer cells.

5

44. A method of performing gene therapy on a patient or a sample, comprising:  
a) contacting cells *in vivo* or *in vitro* with an effective amount of a vector comprising DNA containing at least a portion of BRCA2 sequence selected from the group consisting of SEQ. ID. NO: 4, SEQ. ID. NO: 6, SEQ. ID. NO: 8, SEQ. ID. NO:

10 10, SEQ. ID. NO: 12, or their respective complementary sequences, and

b) allowing the vector to enter the cells,

wherein said patient has a reduced susceptibility for developing a cancer associated with a mutation in the BRCA2 gene.

15 45. A method according to claim 44 wherein said cells include healthy breast, ovarian or pancreatic tissues.

46. A method according to claim 44 wherein a patient has an inherited mutation in the BRCA2 gene.

20

47. A method of treating a patient suspected of having a tumor, comprising:

a) administering to a patient an effective amount of BRCA2 tumor growth inhibitor having an amino acid sequence selected from the group consisting of SEQ. ID. NO: 5, SEQ. ID. NO: 7, SEQ. ID. NO: 9, SEQ. ID. NO: 11, SEQ. ID. NO: 13, any  
25 fragments thereto, and any functional equivalent thereof;

b) allowing the patient's cells to take up the protein, and

c) measuring a reduction in tumor growth.

30 48. The method according to claim 47 wherein said tumor is a breast cancer, an ovarian cancer or a pancreatic cancer.

49. The method according to claim 47 wherein said patient has an inherited mutation in the BRCA2 gene.

50. A method of preventing the formation or growth of a tumor, comprising:
- a) administering to a patient an effective amount of BRCA2 tumor growth inhibiting protein having an amino acid sequence selected from the group consisting of SEQ. ID. NO: 5, SEQ. ID. NO: 7, SEQ. ID. NO: 9, SEQ. ID. NO: 11, SEQ. ID. NO: 13, any fragments thereto, and any functional equivalent thereof; and
  - b) allowing the patient cells to take up the protein.
51. The method according to claim 31 wherein the protein is administered parenternally, by buccal adsorption or inhalation.
52. A cloning vector comprising:
- (a) a DNA sequence as set forth in SEQ. ID. NO: 4, SEQ. ID. NO: 6, SEQ. ID. NO: 8, SEQ. ID. NO: 10, SEQ. ID. NO: 12, or any fragments thereof; and
  - (b) one or more suitable regulatory sequences to induce replication and/or integration in a host cell.
53. An expression vector comprising a DNA sequence as set forth in SEQ. ID. NO: 4, SEQ. ID. NO: 6, SEQ. ID. NO: 8, SEQ. ID. NO: 10, SEQ. ID. NO: 12, or any fragments thereof operatively linked to one or more promoter sequences capable of directing expression of said sequence in a host cell.
54. A host cell transformed with the vector according to claim 52 or 53.
55. A BRCA2 polypeptide which is selected from the group consisting of:
- (a) a fragment of BRCA2 protein sequence as set forth in SEQ. ID. NO: 5, SEQ. ID. NO: 7, SEQ. ID. NO: 9, SEQ. ID. NO: 11, or SEQ. ID. NO: 13;
  - (b) an amino acid sequence which is substantially homologous to the BRCA2 protein sequence as set forth in SEQ. ID. NO: 5, SEQ. ID. NO: 7, SEQ. ID. NO: 9, SEQ. ID. NO: 11, or SEQ. ID. NO: 13;
  - (c) a molecule which has similar function to the BRCA2 protein; and
  - (d) a fusion protein of (a), (b), or (c).

56. An anti-BRCA2 antibody wherein a molecule according to claims 17-21, 23, 25, 27, 29, 31, or 55 is used as an immunogen.

- 5 57. A diagnostic reagent comprising a molecule selected from the group consisting of:
- (a) a DNA sequence as set forth in SEQ. ID. NO: 4, SEQ. ID. NO: 6, SEQ. ID. NO: 8, SEQ. ID. NO: 10, SEQ. ID. NO: 12, or their complementary sequences;
  - (b) a nucleic acid fragment of (a) comprising at least 10 nucleotide in length;
  - 10 (c) a sequence which hybridizes to (a) or (b);
  - (d) a polypeptide according to claim 17-21, 23, 25, 27, 29, 31, or 55; and
  - (e) an antibody which specifically binds to the polypeptide of (d).

- 15 58. A pharmaceutical composition comprising a molecule according to any one of the claims 17-21, 23, 25, 27, 29, 31, 55 in a pharmaceutically acceptable carrier.

59. A pharmaceutical composition comprising a molecule according claim 56 in a pharmaceutically acceptable carrier.

- 20 60. A pharmaceutical composition comprising a molecule according to claim 57 in a pharmaceutically acceptable carrier.

## Figure 1A

## Exon 2

taagtgcattttggtcttctgtttgcagACTTATTTACCAAGCATTGGAGGAATATCGTAGGTAAAA  
ATGCCTATTGGATCCAAAGAGAGGCCAACATTTTTGAAATTTTAAAGACACGCTGC  
AACAAAGCAGgtattgacaaatttatataac

## Exon 3

gggatttttttaaatagATTTAGGACCAATAAGTCTTAATTGGTTTGAAGAACTTTCTTCAG  
AAGCTCCACCTATAATTCTGAACCTGCAGAAGAATCTGAACATAAAAAACAACATT  
ACGAACCAAACCTATTTAAACTCCACAAAGGAAACCATCTTATAATCAGCTGGCTT  
CAACTCCAATAATATTCAAAGAGCAAGGGCTGACTCTGCCGCTGTACCAATCTCCT  
GTAAAGAATTAGATAAATTCAAATTAGACTTAGGtaagtaatgcaataggtagactggg

## Exon 4

tcactgaattattgtactgttcagGAAGGAATGTTCCCAATAGTAGACATAAAAGTCTTCGCACA  
GTGAAACTAAAATGGATCAAGCAGATGATGTTTCCTGTCCACTTCTAAATTCTTGT  
CTTAGTGAAAGGtatgatgaagctattatataaaa

## Exon 5

agggatttgcttgtTTTATTTTAGTCCTGTTGTTCTACAATGTACACATGTAAACACCACAAA  
GAGATAAGTCAGgtatgattaaaaacaatgcttttatctt

## Exon 6

ttaacaattttcccttttttaccctccagTGGTATGTGGGAGTTTGTTTCATACACCAAAGTTTGTG  
AAGgtaaatatt

## Exon 7

taaigatcagggcatttctataaaaaataaactattttcttctccagGGTCGTCAGACACCAAACATATT  
TCTGAAAGTCTAGGAGCTGAGGTGGATCCTGATATGTCTTGGTCAAGTTCTTTAGC  
TACACCACCCACCCTTAGTTCTACTGTGCTCATAGGtaataata

## Exon 8

tttta:cttacagTCAGAAATGAAGAAGCATCTGAAACTGTATTTCTCATGATACTACTGC  
Tgtaagiaaatatgacattgattagact

## Exon 9

ttaactataattttgcagAATGTGAAAAGCTATTTTTCCAATCATGATGAAAGTCTGAAGAAA  
AATGATAGATTTATCGCTTCTGTGACAGACAGTGAAAACACAAATCAAAGAGAAGC  
TGCAAGTCATGgtaagtcctt

## Exon 10

ttaatgtgcttctgttttatactttaacagGATTTGGAAAAACATCAGGGAATTCATTTAAAGTAAATA  
GCTGCAAAGACCACATTGGAAAGTCAATGCCAAATGTCCTAGAAGATGAAGTATAT  
GAAACAGTTGTAGATACCTCTGAAGAAGATAGTTTTTCATTATGTTTTCTAAATGTA  
GAACAAAAAATCTACAAAAAGTAAGAAGTAGCAAGACTAGGAAAAAATTTTCCATG  
AAGCAAACGCTGATGAATGTGAAAAATCTAAAAACCAAGTGAAAGAAAAATACTCAT  
TTGTATCTGAAGTGGAACCAATGATACTGATCCATTAGATTCAAATGTAGCAAATC

Figure 1B

AGAAGCCCTTTGAGAGTGGAAGTGACAAAATCTCCAAGGAAGTTGTACCGTCTTTG  
GCCTGTGAATGGTCTCAACTAACCCTTTTCAGGTCTAAATGGAGCCCAGATGGAGAA  
AATACCCCTATTGCATATTTCTTCATGTGACCAAAATATTTTCAGAAAAAGACCTATTA  
GACACAGAGAACAAAAGAAAGAAAGATTTTCTTACTTCAGAGAATTCTTTGCCACGT  
ATTTCTAGCCTACCAAAATCAGAGAAGCCATTAAATGAGGAAACAGTGGTAAATAA  
GAGAGATGAAGAGCAGCATCTTGAATCTCATACAGACTGCATTCTTGCAGTAAAGC  
AGGCAATATCTGGAAGTCTCCAGTGGCTTCTTCATTTTCAGGGTATCAAAAAGTCTA  
TATTCAGAATAAGAGAATCACCTAAAGAGACTTTCAATGCAAGTTTTTCAGGTCTA  
TGAAGTATCCAACTTTAAAAAAGAACTGAAGCCTCTGAAAGTGGACTGGAAATA  
CATACTGTTTGCTCACAGAAGGAGGACTCCTTATGTCCAAATTTAATTGATAATGGA  
AGCTGGCCAGCCACCACACAGAATTCTGTAGCTTTGAAGAATGCAGGTTTAAAT  
ATCCACTTTGAAAAAGAAAAACAAATAAGTTTATTTATGCTATACATGATGAAACATCT  
TATAAAGGAAAAAAATACCGAAAGACCAAAAATCAGAACTAATTAAGTTCAGCC  
CAGTTTGAAGCAAATGCTTTTGAAGCACCCTTACATTTGCAAATGCTGATTGAGta  
cctctgtct

## Exon 11

tttgtgtttatgttttagGTTTATTGCATTCTTCTGTGAAAAGAAGCTGTTACAGAATGATTCT  
GAAGAACCAACTTTGTCTTAAGTCTCTTTTGGGACAATTCTGAGGAAATGTTCT  
AGAAATGAAACATGTTCTAATAATACAGTAATCTCTCAGGATCTTGATTATAAGAA  
GCAAAATGTAATAAGGAAAACTACAGTTATTTATTACCCAGAAAGCTGATTCTCTG  
TCATGCCTGCAGGAAGGACAGTGTGAAAATGATCCAAAAAGCAAAAAAGTTTCAGA  
TATAAAGAAGAGGTCTTGGCTGCAGCATGTCAACCCAGTACAACATTCAAAAGTGG  
AATACAGTGATACTGACTTTCAATCCCAGAAAAGTCTTTTATATGATCATGAAAATG  
CCAGCACTCTTATTTTAACTCCTACTTCCAAGGATGTTCTGTCAAACCTAGTCTGA  
TTTCTAGAGGCAAAGAATCATACAAAATGTGAGACAAGCTCAAAGGTAACAATTATG  
AATCTGATGTTGAATTAACCAAAAATATTCCCATGGAAAAGAATCAAGATGTATGTG  
CTTTAAATGAAAATTATAAAAACGTTGAGCTGTTGCCACCTGAAAAATACATGAGAG  
TAGCATCACCTTCAAGAAAGGTACAATTCAACCAAAACACAAATCTAAGAGTAATCC  
AAAAAATCAAGAAGAACTACTTCAATTTCAAAAAATACTGTCAATCCAGACTCTG  
AAGAAGCTTTCTCAGACAATGAGAATAATTTGTCTTCCAAGTAGCTAATGAAAGGA  
ATAATCTTGCTTTAGGAAATACTAAGGAAGTTCATGAAACAGACTTGACTTGTGTAA  
ACGAACCCATTTTCAAGAACTCTACCATGGTTTTATATGGAGACACAGGTGATAAAC  
AAGCAACCCAAGTGTCAATTAAGAAAGATTTGGTTTTATGTTCTTGCAGAGGAGAAC  
AAAAATAGTGTAAGCAGCATATAAAAAATGACTCTAGGTCAAGATTTAAATCGGAC  
ATCTCCTTGAATATAGATAAAATACCAGAAAAAATAATGATTACATGAACAAATGG  
GCAGGACTCTTAGGTCCAATTTCAAATCACAGTTTTGGAGGTAGCTTCAGAACAGC  
TTCAAATAAGGAAATCAAGCTCTCTGAACATAACATTAAGAAGAGCAAAATGTTCTT  
CAAAGATATTGAAGAACAATATCCTACTAGTTTAGCTTGTGTTGAAATTGTAAATAC  
CTTGGCATTAGATAATCAAAAGAACTGAGCAAGCCTCAGTCAATTAATACTGTATC  
TGCACATTTACAGAGTAGTGTAGTTGTTTCTGATTGTAAAAATAGTCATATAACCCC  
TCAGATGTTATTTTCCAAGCAGGATTTAATTCAAACCATAATTTAACACCTAGCCAA  
AAGGCAGAAATTACAGAACTTTCTACTATATTAGAAGAATCAGGAAGTCAGTTTGAA  
TTTACTCAGTTTAGAAAACCAAGCTACATATTGCAGAAGAGTACATTTGAAGTGCCT  
GAAAACCAAGATGACTATCTTAAAGACCACTTCTGAGGAATGCAGAGATGCTGATCT  
TCATGTCATAATGAATGCCCATCGATTGGTCAGGTAGACAGCAGCAAGCAATTTG

Figure 1C

AAGGTACAGTTGAAATTAACGGAAGTTTGGCTGGCCTGTTGAAAAATGACTGTAAC  
AAAAGTGCTTCTGGTTATTTAACAGATGAAAATGAAGTGGGGTTTAGGGGCTTTTAT  
TCTGCTCATGGCACAAAACCTGAATGTTTCTACTGAAGCTCTGCAAAAAGCTGTGAA  
ACTGTTTAGTGATATTGAGAATATTAGTGAGGAACTTCTGCAGAGGTACATCCAAT  
AAGTTTATCTTCAAGTAAATGTCATGATTCTGTTGTTTCAATGTTTAAGATAGAAAAT  
CATAATGATAAACTGTAAGTGAAAAAATAATAATGCCAACTGATATTACAAAATA  
ATATTGAAATGACTACTGGCACTTTTGTGGAAGAAATTACTGAAAATTACAAGAGAA  
ATACTGAAAATGAAGATAACAAATATACTGCTGCCAGTAGAAAATTCTCATAACTTAG  
AATTTGATGGCAGTGATTCAAGTAAAAATGATACTGTTTGTATTACATAAAGATGAAA  
CGGACTTGCTATTTACTGATCAGCACACATATGTCTTAAATTATCTGGCCAGTTTA  
TGAAGGAGGGGAAACACTCAGATTAAAGA<sup>\*</sup>GATTTGTGAGATTTAACTTTTTTGGAAAG  
TTGCGAAAGCTCAAGAAGCATGTCATGGTAATACTTCAAATAAAGAACAGTTAACT  
GCTACTAAAACGGAGCAAAATATAAAGATTTTGGAGACTTCTGATACATTTTTTCAG  
ACTGCAAGTGGGAAAAATATTAGTGTGCGCC<sup>4</sup>AAGAGTCATTTAATAAAATTGTAAAT  
TTCTTTGATCAGAAACCAGAAGAAATTGCATAACTTTTCTTAAATTCTGAATTACATT  
CTGACATAAGAAAGAACAATAATGGACATTCTAAGTTATGAGGAAACAGACATAGTT  
AAACACAAAATACTGAAAGAAAGTGTCCAGTTGGTACTGGAAATCACTAGTGAC  
CTTCCAGGGACAACCCGAACGTGATGAAAAGATCAAAGAACCTACTCTGTTGGGT  
TTCATACAGCTAGCGGGAAAAAAGTTAAATTTGCAAAGGAATCTTTGGACAAAGTG  
AAAAACCTTTTTGATGAAAAAGAGCAAGGTACTAGTGAAATCACCAGTTTTAGCCAT  
CAATGGGCAAAGACCCTAAAGTACAGAGAGGCCTGTAAAGACCTTGAATTAGCAT  
GTGAGACCATTGAGATCACAGCTGCCCAAAGTGTAAGAAATGCAGAATTCTCTC  
AATAATGATAAAAACCTTGTCTATTGAGACTGTGGTGCCACCTAAGCTCTTAAGT  
GATAATTTATGTAGACAACTGAAAATCTCAAAACATCAAAAAGTATCTTTTTGAAAG  
TTAAAGTACATGAAAATGTAGAAAAAGAAACAGCAAAAAGTCTCTGCAACTTGTTACA  
CAAATCAGTCCCCCTTATTGAGTCATTGAAAATTCAGCCTTAGCTTTTTACACAAGTT  
GTAGTAGAAAACTTCTGTGAGTCAGACTTCATTACTTGAAGCAAAAAAATGGCTTA  
GAGAAGGAATATTTGATGGTCAACCAGAAAGAATAAATACTGCAGATTATGTAGGA  
AATTATTTGTATGAAAATAATTCAAACAGTACTATAGCTGAAAATGACAAAATCATC  
TCTCCGAAAAACAAGATACTTATTTAAGTAACAGTAGCATGTCTAACAGCTATTCCT  
ACCATTCTGATGAGGTATATAATGATTCAGGATATCTCTCAAAAAATAAACTTGATT  
CTGGTATTGAGCCAGTATTGAAGAATGTTGAAGATCAAAAAAACACTAGTTTTTCCA  
AAGTAATATCCAATGTAAAGATGCAAATGCATACCCACAACTGTAAATGAAGATA  
TTTGCGTTGAGGAACCTTGTGACTAGCTCTTACCCTGCAAAAATAAAATGCAGCC  
ATTAAATTGTCCATATCTAATAGTAATAATTTTGGGTAGGGGCCACCTGC<sup>4</sup>TTTAGG  
ATAGCCAGTGGTAAATCGTTTGTGTTTACATGAAACAATTAAAAAGTGAAAGAC  
ATATTTACAGACAGTTTCAGTAAAGTAATTAAGGAAAAACAACGAGAATAAATCAAAA  
ATTTGCCAAACGAAAATTATGGCAGGTTGTTACGAGGCATTGGATGATTCAGAGGA  
TATTCCTTCACTCTCTAGATAATGATGAATGTAGCAGCATTCACATAAGGTTTTT  
GCTGACATTCAGAGTGAAGAAATTTTACAACATAACCAAAATATGTCTGGATTGGA  
GAAAGTTTTCTAAAATATCACCTTGTGATGTTAGTTTGGAACTTCAGATATATGTAA  
TGTAATATAGGGGAAGCTTCATAAGTCAGTCTCATCTGCAAACTTGTGGGATTTTT  
AGCACAGCAAGTGGAAATCTGTCCAGGTATCAGATGCTTCATTACAAAACGCAAG  
ACAAGTGTCTTCTGAAATAGAAGATAGTACCAAGCAAGTCTTTTCCAAAGTATTGTT  
TAAAAGTAACGAACATTACAGCCAGCTCACAAGAGAAGAAAATACTGCTATACGTA  
CTCCAGAACATTTAATATCCCAAAAAGGCTTTTATATAATGTGGTAAATTCATCTG



## Figure 1D

CTTTCTCTGGATTTAGTACAGCAAGTGGAAAGCAAGTTTCCATTTTAGAAAGTTCCT  
TACACAAAGTTAAGGGAGTGTTAGAGGAATTTGATTTAATCAGAACTGAGCATAGT  
CTTCACTATTACCTACGTCTAGACAAAATGTATCAAAAATACTTCCTCGTGTTGAT  
AAGAGAAACCCAGAGCACTGTGTAAACTCAGAAATGGAAAAACCTGCAGTAAAGA  
ATTTAAATTATCAAATAACTTAAATGTTGAAGGTGGTTCTTCAGAAAATAATCACTCT  
ATTAAAGTTTCTCCATATCTCTCTCAATTTCAACAAGACAAACAACAGTTGGTATTAG  
GAACCAAAGTCTCACTTGTGAGAACATTCATGTTTTGGGAAAAGAACAGGCTTCA  
CCTAAAAACGTAAAAATGGAAATTGGTAAACTGAAACTTTTTCTGATGTTCTGTG  
AAAACAAATATAGAAGTTTGTCTACTTACTCCAAAGATTGAGAAAATACTTTGAAA  
CAGAAGCAGTAGAAATTGCTAAAGCTTTTATGGAAGATGATGAACTGACAGATTCT  
AAACTGCCAGTCATGCCACACATCTCTTTTTACATGTCCCGAAAATGAGGAAATG  
GTTTTGTCAAATTCAGAATTGGAAAAAGAAGAGGAGAGCCCTTATCTTAGTGGgt  
aagtgttcattttaccttcgtgtgccaatca

## Exon 12

aaaacatatatgaaatattcttttagGAGAACCTCAATCAAAAGAACTTATTAAATGAATTTG  
ACAGGATAATAGAAAATCAAGAAAATCCTTAAAGGCTTCAAAAAGCACTCCAGAT  
Ggtaaaattagctttttattata

## Exon 13

aatatgtatataaaataattgttcttagGCACAATAAAAGATCGAAGATTGTTTATGCATCATGT  
TTCTTTAGAGCCGATTACCTGTGTACCCTTTGgtaagacatgtttaaattttctaa

## Exon 14

ccccattgcagCACAACTAAGGAACGTCAAGAGATACAGAATCCAAATTTTACCGCACC  
TGGTCAAGAATTTCTGTCTAAATCTCATTGTATGAACATCTGACTTTGGAAAAATCT  
TCAAGCAATTTAGCAGTTTCAGGACATCCATTTTATCAAGTTTCTGCTACAAGAAAT  
GAAAAAATGAGACACTTGATTACTACAGGCAGACCAACCAAAGTCTTTGTTCCACC  
TTTTAAACTAAATCgCATTTTACAGAGTTGAACAGTGTGTTAGGAATATTAAGTTG  
GAGGAAAACAGACAAAAGCAAAACATTGATGGACATGGCTCTGATGATAGTAAAAA  
TAAGATTAATGACAATGAGATTGATGTTTAAACAAAAACAACCTCCAATCAAGCAGC  
AGCTGTAACCTTACAAAGTGTGAAGAAGAACCTTTAGgtattgtatgacaattgtgtgatgaat

## Exon 15

ttttgctaagtattattctttgatag. TTTAATTACAAGTCTTCAGAATGCCAGAGATATACAGGAT  
ATGCGAATTAAGAAGAAACAAAGGCAACGCGTCTTTCCACAGCCAGGCAGTCTGTA  
TCTTGCAAAAACATCCACTCTGCCTCGAATCTCTCTGAAAGCAGCAGTAGGAGGCC  
AAGTTCCCTCTGCgtgtccccataaacaggtatgtgt

## Exon 16

ttttctttttgtgtgtgtttttttgtgtgtGTGTTCTCATAAACAGCTGTATACGTATGGCGTTTCTAA  
ACATTGCATAAAAATTAACAGCAAAAATGCAGAGTCTTTTCAGTTTCACTGAAGA  
TTATTTTGGTAAGGAAAGTTTATGGACTGGAAAAGGAATACAGTTGGCTGATGGTG  
GATGGCTCATACCCTCCAATGATGGAAAGGCTGGAAAGAAGAAATTTATAGgtactct  
atgcaaaaagattgtgtgttaactttatg

## Figure 1E

## Exon 17

ttattgttcagGGCTCTGTGTGACACTCCAGGTGTGGATCCAAAGCTTATTTCTAGAATTT  
GGGTTTATAATCACTATAGATGGATCATATGGAACTGGCAGCTATGGAATGTGCC  
TTTCCTAAGGAATTTGCTAATAGATGCCTAAGCCCAGAAAGGGTGCTTCTTCAACTA  
AAATACAGgcaagtttaaagcatt

## Exon 18

tttgtttcacttttagATATGATACGGAAATTGATAGAAGCAGAAGATCGGCTATAAAAAAGA  
TAATGGAAAGGGATGACACAGCTGCAAAAACACTTGTTCTCTGTGTTTCTGACATA  
ATTTCAATTGAGCGCAAATATATCTGAACTTCTAGCAATAAACTAGTAGTGCAGAT  
ACCCAAAAAGTGGCCATTATTGAACTTACAGATGGGTGGTATGCTGTTAAGGCCCA  
GTTAGATCCTCCCCTCTTAGCTGTCTTAAAGAATGGCAGACTGACAGTTGGTCAGA  
AGATTATTCTTCATGGAGCAGAACTGGTGGGCTCTCCTGATGCCTGTACACCTCTT  
GAAGCCCCAGAATCTCTTATGTTAAAGgtaaatt

## Exon 19

taaataaatatatttataattgtccagATTTCTGCTAACAGTACTCGGCCTGCTCGCTGGTATAC  
CAAACCTTGGATTCTTTCCTGACCCTAGACCTTTTCTCTGCCCTTATCATCGCTTTT  
CAGTGATGGAGGAAATGTTGTTGTGTTGATGTAATTATTCAAAGAGCATACCCTAT  
ACAGgtatgatgtattcttgaaactta

## Exon 20

tttggtgigttaacacattattacagTGGATGGAGAAGACATCATCTGGATTATACATATTTCCG  
AATGAAAGAGAGGAAGAAAAGCAGCAAAATATGTGGAGGCCCAACAAAAGA  
GACTAGAAGCCTTATTCACATAAAATTCAGGAGGAATTTGAAGAACATGAAGgtaaaatt  
aghtatatggtacacattgttatttc

## Exon 21

agtttagtgaattaataatcctttgttttcttagAAAAACAACAAAACCATATTTACCATCACGTGCAC  
TAACAAGACAGCAAGTTCGTGCTTTGCAAGATGGTGCAGAGCTTTATGAAGCAGTG  
AAGAATGCAGCAGACCCAGCTTACCTTGAGgtgagagagtaagaggacataataatgag

## Exon 22

ttttattccaatcttaaatggtcacagGGTTATTTCACTGAAGAGCAGTTAAGAGCCTTGAATAA  
TCACAGGCAAATGTTGAATGATAAGAAACAAGCTCAGATCCAGTTGGAAATTAGGA  
AGGCCATGGAATCTGCTGAACAAAAGGAACAAGGTTTATCAAGGGATGTCACAAC  
CGTGTGGAAGTTGCGTATTGTAAGCTATTCAAAAAAAGAAAAAGATTTCAGgtaagtatgt  
aaatgctttgtttta

## Exon 23

tctccaaacagTTATACTGAGTATTTGGCGTCCATCATCAGATTTATATTCTCTGTTAACA  
GAAGGAAAGAGATACAGAATTTATCATCTTGCAACTTCAAAATCTAAAAGTAAATCT  
GAAAGAGCTAACATACAGTTAGCAGCGACAAAAAACTCAGTATCAACAACCTACC  
Ggtacaaaccttcattgtaatttt

## Figure 1F

## Exon 24

gaattttgtttgtttctgtagGTTTCAGATGAAATTTTATTTTCAGATTTACCAGCCACGGGAGC  
CCCTTCACTTCAGCAAATTTTATGATCCAGACTTTTCAGCCATCTTGTTCTGAGGTGG  
ACCTAATAGGATTTGTCGTTTCTGTTGTGAAAAAACAGGtaatgcacaatatagtaattttttat  
tgattcttttaaaaaacattgtct

## Exon 25

taacattcttttctttttccattctagGACTTGCCCCCTTTCGTCTATTTGTCAGACGAATGTTACAA  
TTTACTGGCAATAAAGTTTTGGATAGACCTTAATGAGGACATTATTAAGCCTCATAT  
GTTAATTGCTGCAAGCAACCTCCAGTGGCGACCAGAATCCAAATCAGGCCTTCTTA  
CTTTATTTGCTGGAGATTTTCTGTGTTTTCTGCTAGTCCAAAAGAGGGCCACTTTC  
AAGAGACATTCAACAAAATGAAAAATACTGTTGAGGtaaggta

## Exon 26

ataaagcagctttccactattttcttagAATATTGACATACTTTGCAATGAAGCAGAAAACAAGCT  
TATGCATATACTGCATGCAAATGATCCCAAGTGGTCCACCCCACTAAAGACTGTA  
CTTCAGGGCCGTACACTGCTCAAATCATTCTGGTACAGGAAACAAGCTTCTGgtaa  
gttaatgtaaactcaaggaatattataag

## Exon 27

tacgttttcattttttatcagATGTCTTCTCCTAATTGTGAGATATATTATCAAAGTCCTTTATCA  
CTTTGTATGGCCAAAAGGAAGTCTGTTTCCACACCTGTCTCAGCCCAGATGACTTC  
AAAGTCTTGTAAGGGGAGAAAGAGATTGATGACCAAAAGAACTGCAAAAAGAGAA  
GAGCCTTGGATTTCTTGAGTAGACTGCCTTTACCTCCACCTGTTAGTCCCATTTGTA  
CATTTGTTTCTCCGGCTGCACAGAAGGCATTTTCAGCCACCAAGGAGTTGTGGCAC  
CAAATACGAAACACCCATAAAGAAAAAAGAACTGAATTCTCCTCAGATGACTCCATT  
TAAAAAATTCATGAAATTTCTCTTTTGAAAGTAATTCAATAGCTGACGAAGAAGTT  
GCATTGATAAATACCCAAGCTCTTTTGTCTGGTTCAACAGGAGAAAAACAATTTATA  
TCTGTCAGTGAATCCACTAGGACTGCTCCCACAGTTCAGAAGATTATCTCAGACT  
GAAACGACGTTGTACTACATCTCTGATCAAAGAACAGGAGAGTTCCCAGGCCAGTA  
CGGAAGAATGTGAGAAAAATAAGCAGGACACAATTACAATAAAAAATATATCTAA  
GCATTTGCAAAGGCGACAATAAATTATTGACGCTTAACCTTTCAGTTTATAAGACT  
GGA

## Figure 2A

## Exon 2

taagtgcattttggtcttctgtttgcagACTTATTTACCAAGCATTGGAGGAATATCGTAGGTAAAA  
ATGCCTATTGGATCCAAAGAGAGGCCAACATTTTTTGAATTTTAAAGACACGCTGC  
AACAAAGCAGgtattgacaaatttatataac

## Exon 3

gggatttttttaaatagATTTAGGACCAATAAGTCTTAATTGGTTTGAAGAACTTTCTTCAG  
AAGCTCCACCCTATAATTCTGAACCTGCAGAAGAATCTGAACATAAAAAACAACAATT  
ACGAACCAAACCTATTTAAACTCCACAAAGGAAACCATCTTATAATCAGCTGGCTT  
CAACTCCAATAATATTCAAAGAGCAAGGGCTGACTCTGCCGCTGTACCAATCTCCT  
GTAAAAGAATTAGATAAATTCAAATTAGACTTAGGtaagtaatgcaatatggtagactggg

## Exon 4

tcactgaattattgtactgtttcagGAAGGAATGTTCCCAATAGTAGACATAAAAGTCTTCGCACA  
GTGAAAACTAAAATGGATCAAGCAGATGATGTTTCCTGTCCACTTCTAAATTCTTGT  
CTTAGTGAAAGgtatgatgaagctattatataaaa

## Exon 5

acggatttgctttgtttatttttagTCCTGTTGTTCTACAATGTACACATGTAACACCACAAAGAG  
ATAAGTCAGgtatgattaaaaacaatgcttttattctt

## Exon 6

ttaacaattttcccttttttacccccagTGGTATGTGGGAGTTTGTTTCATACACCAAAGTTTGTG  
AAGgtaaatatt

## Exon 7

taatgatcagggcattttctataaaaaataaaactattttcttctccagGGTCGTCAGACACCAAAACATATT  
TCTGAAAGTCTAGGAGCTGAGGTGGATCCTGATATGTCTTGGTCAAGTTCCTTAGC  
TACACCACCCACCCTTAGTTCTACTGTGCTCATAGgtataata

## Exon 8

tttatcttacagTCAGAAATGAAGAAGCATCTGAAACTGTATTTCTCATGATACTACTGC  
Tgtaagtaaatatgacattgattagact

## Exon 9

ttaaactataattttgcagAATGTGAAAAGCTATTTTTCCAATCATGATGAAAGTCTGAAGAAA  
AATGATAGATTTATCGCTTCTGTGACAGACAGTGAAAACACAAATCAAAGAGAAGC  
TGCAAGTCATGgtaagtcctt

## Exon 10

taaatgtgcttctgtttatacttaacagGATTTGGAAAAACATCAGGGAATTCATTTAAAGTAAATA  
GCTGCAAAGACCACATTGGAAAGTCAATGCCAAATGTCCTAGAAGATGAAGTATAT  
GAAACAGTTGTAGATACCTCTGAAGAAGATAGTTTTTTCATTATGTTTTCTAAATGTA  
GAACAAAAAATCTACAAAAAGTAAGAACTAGCAAGACTAGGAAAAAAATTTCCATG  
AAGCAAACGCTGATGAATGTGAAAAATCTAAAAACCAAGTGAAAGAAAAATACTCAT  
TTGTATCTGAAGTGGAACCAATGATACTGATCCATTAGATTCAAATGTAGCAAATC

Figure 2B

AGAAGCCCTTTGAGAGTGGAAGTGACAAAATCTCCAAGGAAGTTGTACCGTCTTTG  
GCCTGTGAATGGTCTCAACTAACCCTTTTCAGGTCTAAATGGAGCCCAGATGGAGAA  
AATACCCCTATTGCATATTTCTTCATGTGACCAAAATATTTTCAGAAAAAGACCTATTA  
GACACAGAGAACAAAAGAAAGAAAGATTTTCTTACTTCAGAGAATTCTTTGCCACGT  
ATTTCTAGCCTACCAAAATCAGAGAAGCCATTAAATGAGGAAACAGTGGTAAATAA  
GAGAGATGAAGAGCAGCATCTTGAATCTCATACAGACTGCATTCTTGCAGTAAAGC  
AGGCAATATCTGGAACCTTCTCCAGTGGCTTCTTCATTTTCAGGGTATCAAAAAGTCTA  
TATTCAGAATAAGAGAATCACCTAAAGAGACTTTCAATGCAAGTTTTTTCAGGTCATA  
TGA CTGATCCAACTTTAAAAAGAAACTGAAGCCTCTGAAAGTGGACTGGAAATA  
CATACTGTTTGCTCACAGAAGGAGGACTCCTTATGTCCAAATTTAATTGATAATGGA  
AGCTGGCCAGCCACCACCACACAGAATTCGTAGCTTTGAAGAATGCAGGTTTAAAT  
ATCCACTTTGAAAAAGAAAACAAATAAGTTTATTTATGCTATACATGATGAAACATCT  
TATAAAGGAAAAAAATACCGAAAGACCAAAAATCAGAACTAATTAAGTTCAGCC  
CAGTTTGAAGCAAATGCTTTTGAAGCACCACATACATTTGCAATGCTGATTCAAGT  
accctgtct

## Exon 11

tttggtttttatggttagGTTTATTGCATTCTTCTGTGAAAAGAAGCTGTTTCACAGAATGATTCT  
GAAGAACCAACTTTGTCTTAAGTCTTTTGGGACAATTCTGAGGAAATGTTCT  
AGAAATGAAACATGTTCTAATAATACAGTAATCTCTCAGGATCTTGATTATAAAGAA  
GCAAAATGTAATAAGGAAAACTACAGTTATTTATTACCCAGAAAGCTGATTCTCTG  
TCATGCCTGCAGGAAGGACAGTGTGAAAATGATCCAAAAAGCAAAAAAGTTTCAGA  
TATAAAGAAGAGGTCTTGGCTGCAGCATGTCACCCAGTACAACATTCAAAGTGG  
AATACAGTGATACTGACTTTCAATCCAGAAAAGTCTTTTATATGATCATGAAAATG  
CCAGCACTCTTATTTTAACTCCTACTTCCAAGGATGTTCTGTCAAACCTAGTCATGA  
TTTCTAGAGGCAAAAGAAATCATACAAAATGTCAGACAAGCTCAAAGGTAACAATTATG  
AATCTGATGTTGAATTAAACCAAAATATTCCCATGGAAAAGAAATCAAGATGTATGTG  
CTTTAAATGAAAATTATAAAAAACGTTGAGCTGTTGCCACCTGAAAAATACATGAGAG  
TAGCATCACCTTCAAGAAAGGTACAATTCAACCAAAACACAAATCTAAGAGTAATCC  
AAAAAATCAAGAAGAACTACTTCAATTTCAAAAATAACTGTCAATCCAGACTCTG  
AAGAACTTTTCTCAGACAATGAGAATAATTTTGTCTTCCAAGTAGCTAATGAAAGGA  
ATAATCTTGCTTTAGGAAATACTAAGGAACTTCATGAAACAGACTTGACTTGTGTAA  
ACGAACCCATTTTCAAGAAGTCTACCATGGTTTATATGGAGACACAGGTGATAAAC  
AAGCAACCCCAAGTGTCAATTAAAAAAGATTTGGTTTATGTTCTTGCAGAGGAGAAC  
AAAAATAGTGTAAGCAGCATATAAAAATGACTCTAGGTCAAGATTTAAAAACGGAC  
ATCTCCTTGAATATAGATAAAAATACCAGAAAAAATAATGATTACATGAACAAATGG  
GCAGGACTCTTAGGTCCAATTTCAAATCACAGTTTTTGGAGGTAGCTTCAGAACAGC  
TTCAAATAAGGAAATCAAGCTCTCTGAACATAACATTAAGAAGAGCAAAATGTTCTT  
CAAAGATATTGAAGAACAAATATCCTACTAGTTTAGCTTGTGTTGAAATTGTAAATAC  
CTTGGCATTAGATAATCAAAAGAACTGAGCAAGCCTCAGTCAATTAATACTGTATC  
TGCACATTTACAGAGTAGTGTAGTTGTTTCTGATTGTAAAAATAGTCATATAACCCC  
TCAGATGTTATTTTCCAAGCAGGATTTTAAATCAAACCATATTTAACACCTAGCCAA  
AAGGCAGAAATTACAGAAGCTTTCTACTATATTAGAAGAAATCAGGAAGTCAGTTTGAA  
TTTACTCAGTTTAGAAAACCAAGCTACATATTGCAGAAGAGTACATTTGAAGTGCCT  
GAAAACCAAGATGACTATCTTAAAGACCACTTCTGAGGAATGCAGAGATGCTGATCT  
TCATGTCATAATGAATGCCCCATCGATTGGTCAGGTAGACAGCAGCAAGCAATTTG

Figure 2C

AAGGTACAGTTGAAATTAACGGAAGTTTGCTGGCCTGTTGAAAAATGACTGTAAC  
AAAAGTGCTTCTGGTTATTTAACAGATGAAAATGAAGTGGGGTTTAGGGGCTTTTAT  
TCTGCTCATGGCACAAAAGTGAATGTTTCTACTGAAGCTCTGCAAAAAGCTGTGAA  
ACTGTTTAGTGATATTGAGAATATTAGTGAGGAACTTCTGCAGAGGTACATCCAAT  
AAGTTTATCTTCAAGTAAATGTCATGATTCTGTTGTTTCAATGTTTAAGATAGAAAAT  
CATAATGATAAACTGTAAGTGAAAAAATAATAAATGCCAACTGATATTACAAAATA  
ATATTGAAATGACTACTGGCACTTTTGTGGAAGAAATTACTGAAAATTACAAGAGAA  
ATACTGAAAATGAAGATAACAAATATACTGCTGCCAGTAGAAAATTCTCATAACTTAG  
AATTTGATGGCAGTGATTCAAGTAAAAATGATACTGTTTGTATTCTATAAGATGAAA  
CGGACTTGCTATTTACTGATCAGCACACATATGTCTTAAATTATCTGGCCAGTTTA  
TGAAGGAGGGGAAACACTCAGATTAAGAAGATTTGTCAGATTTAACTTTTTTGGAAAG  
TTGCCAAAGCTCAAGAAGCATGTCATGGTAATACTTCAAATAAAGAACAGTTAACT  
GCTACTAAAACGGAGCAAAATATAAAGATTTTGAGACTTCTGATACATTTTTTTCAG  
ACTGCAAGTGGGAAAAATATTAGTGTGCCAAAGAGTCATTTAATAAAATTGTAAAT  
TTCTTTGATCAGAAACCAGAAGAATTGCATAACTTTTCTTAAATTCTGAATTACATT  
CTGACATAAGAAAGAACAAAATGGACATTCTAAGTTATGAGGAAACAGACATAGTT  
AAACACAAAATACTGAAAGAAAGTGTCCCAGTTGGTACTGGAAATCAACTAGTGAC  
CTTCCAGGGACAACCCGAACGTGATGAAAAGATCAAAGAACCCTACTCTGTTGGGTT  
TTCATACAGCTAGCGGGAAAAAAGTTAAAATTGCAAAGGAATCTTTGGACAAAGTG  
AAAAACCTTTTTGATGAAAAAGAGCAAGGTACTAGTGAAATCACCAGTTTTAGCCAT  
CAATGGGCAAAGACCCTAAAGTACAGAGAGGCCTGTAAAGACCTTGAATTAGCAT  
GTGAGACCATTGAGATCACAGCTGCCCCAAAGTGTAAAGAAATGCAGAATTCTCTC  
AATAATGATAAAAACCTTGTTTCTATTGAGACTGTGGTGCCACCTAAGCTCTTAAGT  
GATAATTTATGTAGACAACTGAAAATCTCAAAACATCAAAAAGTATCTTTTGAAAG  
TTAAAGTACATGAAAATGTAGAAAAAGAAACAGCAAAAAGTCCCTGCAACTTGTTACA  
CAAATCAGTCCCCTTATTCAGTCATTGAAAATTCAGCCTTAGCTTTTTACACAAGTT  
GTAGTAGAAAACTTCTGTGAGTCAGACTTCATTACTTGAAGCAAAAAAATGGCTTA  
GAGAAGGAATATTTGATGGTCAACCAGAAAGAAATAAATACTGCAGATTATGTAGGA  
AATTATTTGTATGAAAATAATTCAAACAGTACTATAGCTGAAAATGACAAAAATCATC  
TCTCCGAAAAACAAGATACTTATTTAAGTAACAGTAGCATGTCTAACAGCTATTCT  
ACCATTTCTGATGAGGTATATAATGATTCAGGATATCTCTCAAAAAATAAATTGATT  
CTGGTATTGAGCCAGTATTGAAGAATGTTGAAGATCAAAAAAACACTAGTTTTTCCA  
AAGTAATATCCAATGTAAAAGATGCAAATGCATACCCACAACTGTAAATGAAGATA  
TTTGCGTTGAGGAACTTGTGACTAGCTCTTCAACCCTGCAAAAATAAAAATGCAGCC  
ATTAATTTGTCCATATCTAATAGTAATAATTTTGAGGTAGGGCCACCTGCATTTAGG  
ATAGCCAGTGGTAAAATCGTTTGTGTTTACATGAAACAATTAAAAAGTGAAAGAC  
ATATTTACAGACAGTTTTCAGTAAAGTAATTAAGGAAAACAACGAGAATAAATCAAAA  
ATTTGCCAAACGAAAATTATGGCAGGTTGTTACGAGGCATTGGATGATTCAGAGGA  
TATTTCTCATAACTCTCTAGATAATGATGAATGTAGCACGCATTCACATAAGGTTTT  
GCTGACATTGAGAGTGAAGAAATTTTACAACATAACCAAAATATGTCTGGATTGGA  
GAAAGTTTCTAAAATATCACCTTGTGATGTTAGTTTGGAACTTCAGATATATGTAAA  
TGTAAGTATAGGGAAGCTTCATAAGTCAGTCTCATCTGCAAACTTGTGGGATTTTT  
AGCACAGCAAGTGGAAAATCTGTCCAGGTATCAGATGCTTCATTACAAAACGCAAG  
ACAAGTGTCTTCTGAAATAGAAGATAGTACCAAGCAAGTCTTTTCCAAAGTATTGTT  
TAAAAGTAACGAACATTCAGACCAGCTCACAAGAGAAGAAAATACTGCTATACGTA  
CTCCAGAACATTTAATATCCCAAAAAGGCTTTTCATATAATGTGGTAAATTCATCTG

Figure 2D

CTTTCTCTGGATTTAGTACAGCAAGTGGAAAGCAAGTTTCCATTTTAGAAAAGTTCCCT  
TACACAAAGTTAAGGGAGTGTAGAGGAATTTGATTTAATCAGAACTGAGCATAGT  
CTTCACTATTCACCTACGTCTAGACAAAATGTATCAAAAATACTTCCTCGTGTTGAT  
AAGAGAAAACCCAGAGCACTGTGTAAACTCAGAAATGGAAAAAACCTGCAGTAAAGA  
ATTTAAATTATCAAATAACTTAAATGTTGAAGGTGGTTCTTCAGAAAATAATCACTCT  
ATTAAGTTTCTCCATATCTCTCTCAATTTCAACAAGACAAACAACAGTTGGTATTAG  
GAACCAAAGTCTCACTTGTGAGAACATTCATGTTTTGGGAAAAGAACAGGCTTCA  
CCTAAAAACGTAAAAATGGAAATTGGTAAACTGAACTTTTTCTGATGTTCCCTGTG  
AAAACAAATATAGAAGTTTGTCTACTTACTCCAAAGATTCAGAAAATACTTTGAAA  
CAGAAGCAGTAGAAATTGCTAAAGCTTTTATGGAAGATGATGAACTGACAGATTCT  
AAACTGCCAAGTCATGCCACACATTCTCTTTTACATGTCCCGAAAATGAGGAAATG  
GTTTTGTCAAATTCAGAATTGGAAAAAGAAGAGGAGAGCCCTTATCTTAGTGgt  
aagtgttcattttaccttcgtgttgccaatca

## Exon 12

aaaacatatatgaaatatttcttttagGAGAACCCTCAATCAAAAGAACTTATTAATGAATTG  
ACAGGATAATAGAAAATCAAGAAAAATCCTTAAAGGCTTCAAAAGCACTCCAGAT  
Ggtaaaatagctttttattata

## Exon 13

aatatgtaataaaaaataatgtttcctagGCACAATAAAAGATCGAAGATTGTTTATGCATCATGT  
TTCTTTAGAGCCGATTACCTGTGTACCCTTTCGgtaagacatgtttaaattttctaa

## Exon 14

ccccattgcagCACAACTAAGGAACGTCAAGAGATACAGAATCCAAATTTTACCGCACC  
TGGTCAAGAATTTCTGTCTAAATCTCATTTGTATGAACATCTGACTTTGGAAAAATCT  
TCAAGCAATTTAGCAGTTTCAGGACATCCATTTTATCAAGTTTCTGCTACAAGAAAT  
GAAAAAATGAGACACTTGATTACTACAGGCAGACCAACCAAGTCTTTGTTCCACC  
TTTTAAACTAAATCACATTTTCACAGAGTTGAACAGTGTGTTAGGAATATTAAGTTG  
GAGGAAAACAGACAAAAGCAAAACATTGATGGACATGGCTCTGATGATAGTAAAAA  
TAAGATTAATGACAATGAGATTCATCAGTTTAAACAAAACAACCTCCAATCAAGCAGC  
AGCTGTAACTTTCACAAAGTGTGAAGAAGAACCTTTAGgtattgtatgacaatttgtgtgatgaatt

## Exon 15

ttttgctaagtatttattctttgatagATTTAATTACAAGTCTTCAGAATGCCAGAGATATACAGGAT  
ATGCGAATTAAGAAGAAACAAAGGCAACGCGTCTTCCACAGCCAGGCAGTCTGTA  
TCTTGCAAAAACATCCACTCTGCCTCGAATCTCTCTGAAAGCAGCAGTAGGAGGCC  
AAGTTCCCTCTGCGTGTTCTCATAAACAGgtatgtgt

## Exon 16

ttttctttttgtgtgtttatttctgttagCTGTATACGTATGGCGTTTCTAAACATTGCATAAAAATTA  
ACAGCAAAAATGCAGAGTCTTTTCAGTTTCACACTGAAGATTATTTTGGTAAGGAAA  
GTTTATGGACTGGAAAAGGAATACAGTTGGCTGATGGTGGATGGCTCATACCCTCC  
AATGATGGAAAGGCTGGAAAAGAAGAATTTTATAGgtactctatgcaaaaagattgtgtgttaacttt  
atg

## Figure 2E

## Exon 17

ttattgttcagGGCTCTGTGTGACACTCCAGGTGTGGATCCAAAGCTTATTTCTAGAATTT  
GGGTTTATAATCACTATAGATGGATCATATGGAACTGGCAGCTATGGAATGTGCC  
TTTCCTAAGGAATTTGCTAATAGATGCCTAAGCCCAGAAAGGGTGCTTCTTCAACTA  
AAATACAGgcaagtttaagcatt

## Exon 18

tttgtttcacttttagATATGATACGGAAATTGATAGAAGCAGAAGATCGGCTATAAAAAAGA  
TAATGGAAAGGGATGACACAGCTGCAAAAACACTTGTTCTCTGTGTTTCTGACATA  
ATTTCAATTGAGCGCAAATATATCTGAACTTCTAGCAATAAACTAGTAGTGACAGAT  
ACCCAAAAAGTGGCCATTATTGAACTTACAGATGGGTGGTATGCTGTTAAGGCCCA  
GTTAGATCCTCCCCTCTTAGCTGTCTTAAAGAATGGCAGACTGACAGTTGGTCAGA  
AGATTATTCTTCATGGAGCAGAACTGGTGGGCTCTCCTGATGCCTGTACACCTCTT  
GAAGCCCCAGAATCTCTTATGTTAAAGgtaaatt

## Exon 19

tzaatcaatatatttataattgtccagATTTCTGCTAACAGTACTCGGCCTGCTCGCTGGTATAC  
CAAACCTTGGATTCTTTCTGACCCTAGACCTTTTCTCTGCCCTTATCATCGCTTTT  
CAGTGATGGAGGAAATGTTGGTGTGTTGATGTAATTATTCAAAGAGCATACCCTAT  
ACAGgtatgatgtattcttgaaactta

## Exon 20

tttggtgtgtgtaacacattattacagTGGATGGAGAAGACATCATCTGGATTATACATATTTTCG  
AATGAAAGAGAGGAAGAAAAGGAAGCAGCAAAATATGTGGAGGCCCAACAAAAGA  
GACTAGAAGCCTTATTCATAAAATTGAGGAGGAATTTGAAGAACATGAAGgtaaaatt  
agtatatggtacacattgttatttc

## Exon 21

agtttagtgaattaataatcctttgttttcttagAAAACACAACAAACCATATTTACCATCACGTGCAC  
TAACAAGACAGCAAGTTCGTGCTTTGCAAGATGGTGCAGAGCTTTATGAAGCAGTG  
AAGAATGCAGCAGACCCAGCTTACCTTGAGgtgagagagtaagaggacataatgag

## Exon 22

ttttattccaatatcttaaatggtcacagGGTTATTTCAAGTGAAGAGCAGTTAAGAGCCTTGAATAA  
TCACAGGCCAAATGTTGAATGATAAGAAACAAGCTCAGATCCAGTTGGAAATTAGGA  
AGGCCATGGAATCTGCTGAACAAAAGGAACAAGGTTTATCAAGGGATGTCACAACC  
GTGTGGAAGTTGCGTATTGTAAGCTATTCAAAAAAGAAAAAGATTGAGgtaagatgia  
aatgctttgttttta

## Exon 23

tctccaaacagTTATACTGAGTATTTGGCGTCCATCATCAGATTTATATTCTCTGTTAACA  
GAAGGAAAGAGATACAGAATTTATCATCTTGCAACTTCAAAATCTAAAAGTAAATCT  
GAAAGAGCTAACATACAGTTAGCAGCGACAAAAAAACTCAGTATCAACAACTACC  
Ggtacaaaccttcattgtaatttt



## Figure 2F

## Exon 24

gaatgtttgtttgtttctgtagGTTTCAGATGAAATTTTATTTTCAGATTACCAGCCACGGGAGC  
CCCTTCACTTCAGCAAATTTTATAGATCCAGACTTTTCAGCCATCTTGTTCTGAGGTGG  
ACCTAATAGGATTTGTCGTTTCTGTTGTGAAAAAACAGglaatgcacaatatagtaattttttat  
tgattcttttaaaaaacattgtct

## Exon 25

taacattcttttctttttccattctagGACTTGCCCCTTTCGTCTATTTGTCAGACGAATGTTACAA  
TTTACTGGCAATAAAGTTTTGGATAGACCTTAATGAGGACATTATTAAGCCTCATAT  
GTTAATTGCTGCAAGCAACCTCCAGTGGCGACCAGAATCCAAATCAGGCCTTCTTA  
CTTTATTTGCTGGAGATTTTCTGTGTTTTCTGCTAGTCCAAAAGAGGGCCACTTTC  
AAGAGACATTCAACAAAATGAAAAATACTGTTGAGgtaaggta

## Exon 26

ataaagcagcttttccactattttcttagAATATTGACATACTTTGCAATGAAGCAGAAAACAAGCT  
TATGCATATACTGCATGCAAATGATCCCAAGTGGTCCACCCCACTAAAGACTGTA  
CTTCAGGGCCGTACACTGCTCAAATCATTCTGCTGGTACAGGAAACAAGCTTCTGgtaa  
gttaatgtaaactcaaggaatattataag

## Exon 27

tacgttttcattttttatcagATGTCTTCTCCTAATTGTGAGATATATTATCAAAGTCCTTTATCA  
CTTTGTATGGCCAAAAGGAAGTCTGTTTCCACACCTGTCTCAGCCCAGATGACTTC  
AAAGTCTTGTAAGGGGAGAAAGAGATTGATGACCAAAGAAGTGCAAAAAGAGAA  
GAGCCTTGGATTCTTGAGTAGACTGCCTTTACCTCCACCTGTTAGTCCCATTGTGA  
CATTTGTTTCTCCGGCTGCACAGAAGGCATTTTCAGCCACCAAGGAGTTGTGGCAC  
CAAATACGAAACACCCATAAAGAAAAAAGAAGTGAATTCTCCTCAGATGACTCCATT  
TAAAAAATTCAATGAAATTTCTCTTTTGGAAAGTAATTCAATAGCTGACGAAGAAGT  
GCATTGATAAATACCCAAGCTCTTTTGTCTGGTTCAACAGGAGAAAAACAATTTATA  
TCTGTCACTGAATCCACTAGGACTGCTCCACCAAGTTCAGAAGATTATCTCAGACT  
GAAACGACGTTGTACTACATCTCTGATCAAAGAACAGGAGAGTTCCCAGGCCAGTA  
CGGAAGAATGTGAGAAAAATAAGCAGGACACAATTACAATAAAAAATATATCTAA  
GCATTTGCAAAGGCGACAATAAATTATTGACGCTTAACCTTTCCAGTTTATAAGACT  
GGA



# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 98/16905

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 6 C12N15/12 C07K14/47 C12Q1/68 A61K48/00 C07K16/18  
A61K38/17

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 6 C12N C07K C12Q A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GB 2 307 477 A (CANCER RES CAMPAIGN TECHNOLOGY LTD ; DUKE UNIVERSITY) 28 May 1997 see figure 7, underlined sequences on sheets 20/52, 27/52 and 31/52 ---	1,9, 55-60
X	TAFTIGIAN S V ET AL: "The complete BRCA2 gene and mutations in chromosome 13q-linked kindreds" NATURE GENETICS, vol. 3, no. 12, March 1996, pages 333-337, XP002076942 cited in the application see table 1C --- -/--	1-16, 32-39

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

27 January 1999

Date of mailing of the international search report

02/02/1999

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# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 98/16905

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 22689 A (MYRIAD GENETICS INC ;UNIV PENNSYLVANIA (US); HSC RESEARCH & DEV LI) 26 June 1997 see SEQ ID NO:1 especially nucleotides 643-666 on page 90 and nucleotides 5782-5790 on page 98. ---	9,55-60
P,X	WO 97 30108 A (VANDERBILT UNIVERSITY; UNIVERSITY OF WASHINGTON) 21 August 1997 see SEQ ID NO:3 nucleotides 623-634, 5751-5759 and 7794-7834, for claim 9 see also nucleotides 616-634. -----	1,9

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 98/ 16905

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Remark: Although claims 41-43 and 46-51 and partially claims 44 and 45 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the vector.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

information on patent family members

International Application No

PCT/US 98/16905

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
GB 2307477 A	28-05-1997	AU 7635096 A	11-06-1997
		CA 2238010 A	29-05-1997
		EP 0858467 A	19-08-1998
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WO 9722689 A	26-06-1997	US 5837492 A	17-11-1998
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		CA 2239733 A	26-06-1997
		EP 0785216 A	23-07-1997
		NO 982785 A	17-08-1998
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